**Supplementary materials**

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**Manuscript title: "Scalable syntheses of traceable ribosylated $NAD^+$ precursors"**

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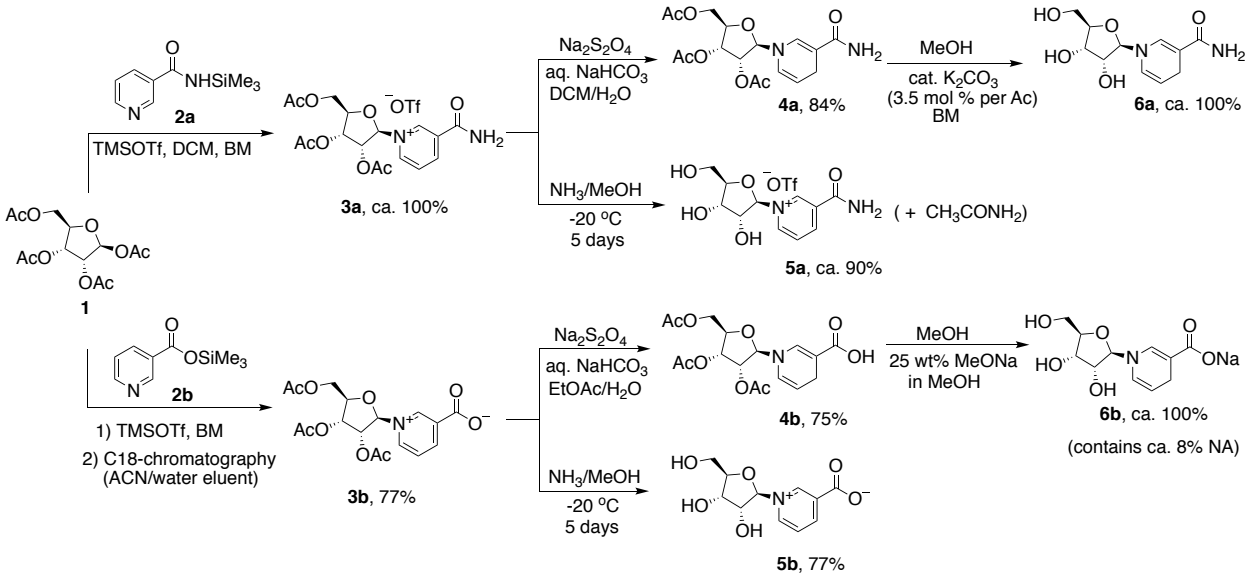
## EXPERIMENTAL




**Scheme 1S.** Chemical syntheses of $NAD^+$ precursors.

**General remarks.** NMR spectra were recorded on a Bruker Avance III HD 400 spectrometer ($^{1}H$, 400.11; $^{19}F$, 376.44; and $^{13}C$, 100.62 MHz) using residual proton signal ($^{1}H$) and that of carbon atom ($^{13}C$) of a deuterated solvent as an internal standard relative to TMS, and $CFCl_3$ ($^{19}F$) as an external standard. Column chromatography was performed on silica gel columns using medium pressure liquid chromatography systems (Biotage or Teledyne) with UV monitoring of eluted fractions (at 280 nm and 350 nm). Analytical TLCs were performed with Merck silica gel 60 F254 plates; visualization of TLCs was accomplished by UV light. HRMS spectra were obtained on a LTQ Orbitrap XL Mass Spectrometer (HESI source, positive polarity, capillary temp 200°C, source voltage 3.0 kV).

All commercial reagents and solvents were purchased from VWR and used without further purification. Anhydrous DCM was obtained by distillation of commercial DCM over calcium hydride. Anhydrous commercial DMF was kept over calcinated molecular sieves. Anhydrous MeOH was prepared by distillation over Mg in the presence of iodine according to standard procedure and kept afterwards over molecular sieves. [$^{18}O$]Water (97% $^{18}O$) and potassium

[$^{13}$C]cyanide (99% $^{13}$C) were purchased from Cambridge Isotope Laboratories, D-[UL-$^{13}C_5$]ribose (99% $^{13}$C) was purchased from Omicron Biochemicals.

Compounds **3a**,[1] **4a**,[1] **5a**,[2] **6a**,[1] **3b**,[3] **4b**,[3] **5b**,[4] and **6b**[3] were previously described in literature, and their $^1$H and $^{13}$C NMR spectral characteristics correspond to those previously reported. For the synthesis of [$^{13}$C-*nitrile*]nicotinonitrile (**14**), method described in ref.[5] was adopted. For the synthesis of $^{18}$O-labelled amides **7** and **15**, method reported in ref.[6] was applied. 1,2,3,5-Tetra-*O*-acetyl-α/β-D-[$^{13}C_5$]ribofuranose ([$^{13}C_5$]RTA, **9**) was synthesized from commercially available [$^{13}C_5$]ribose (Omicron Biochemicals, LLC) according to procedure described in ref.[7,8] Assignment of peaks of corresponding carbon and proton atoms in the $^1$H and $^{13}$C NMR spectra of the isotopically labelled 1,2,3,5-tetra-*O*-acetyl-α/β-D-[$^{13}C_5$]ribofuranose was made on the basis of ref.[8]

***N*-(Trimethylsilyl)nicotinamide (2a).** A 100 mL round-bottom two-neck flask equipped with a reflux condenser was charged with nicotinamide (5.00 g; 0.041 mol) followed by addition of HMDS (34.3 mL; 26.4 g; 0.164 mol; 4 equiv.) *via* a syringe in one portion. Ammonium sulfate (0.007 g) was added to the mixture and the reaction mixture was heated in an oil bath to 110-120°C (oil bath temperature) at intensive stirring. Gas evolution started at ca. 115°C and dissolution completed at ca. 120°C after 3-4 hours of reacting. The reaction solution was left stirred at 110-115°C for 2 days. After completion of the reaction (control by $^1$H NMR), the reaction mixture was allowed to cool down to room temperature and was transferred in a round-bottom single-neck flask and evaporated to dryness on a rotary evaporator followed by drying under high vacuum to give a cream-colored solid, 7.36 g (93%). $^1$H NMR ($CDCl_3$), δ, ppm: 0.31 (br s, 9H, $SiMe_3$), 5.72 (br s, 1H, NH), 7.32 (dd, 1H, $^3J_{HH}$= 4.8 Hz, $^3J_{HH}$= 8.0 Hz, H5), 8.09 (dt, 1H, $^3J_{HH}$= 7.9 Hz, $^4J_{HH}$= 2.0 Hz, H4), 8.66 (dd, 1H, $^3J_{HH}$= 4.9 Hz, $^4J_{HH}$= 1.6 Hz, H6), 8.95 (d, 1H, $^4J_{HH}$= 2.2 Hz, H2). $^{13}$C NMR ($CDCl_3$), δ, ppm: 0.00 ($SiMe_3$), 124.09 (C5), 131.31 (C3), 135.99 (C4), 149.05 (C2), 153.00 (C6), 170.99 (CO).

**3-Carbamoyl-1-((2R,3R,4R,5R)-3,4-diacetoxy-5-(acetoxymethyl)tetrahydrofuran-2-yl)pyridin-1-ium trifluoromethanesulfonate (NRTA OTf, 3a).** A PTFE jar was charged with silylated nicotinamide **2a** (0.80 g; 0.004 mol), 1,2,3,5-tetra-*O*-acetyl-D-β-ribofuranose **1** (1.31 g; 0.004 mol) and anhydrous DCM (0.4 mL; 0.006 mol) was added, followed by addition of TMSOTf (1.13 g; 0.005 mol). The reagents were subjected to ball-milling on a Retsch MM400 miller for 30 min at 30 Hz. The jar was allowed to cool down to room temperature. The content of the jar was dissolved in DCM (2×10 mL) and the yellow solution was transferred into a round bottom flask. Volatiles were removed on a rotary evaporator to dryness to give a yellow foam (2.92 g; ca. quantitative yield as calculated on N-silylated form of **4**) triturated by a spatula resulting in a yellow powder. The product containing residues of acetic acid and silylated residues was used on the next step without additional purification. $^{19}$F NMR ($D_2O$), δ, ppm: -78.83. $^1$H NMR ($D_2O$), δ, ppm: 1.95 (Me from acetic acid residue), 2.02 (s, 3H, Me), 2.06 (s, 3H, Me), 2.09 (s, 3H, Me), 4.42–4.50 (m, 2H, H5′), 4.80–4.83 (m, 1H, H4′), 5.38 (apparent t, 1H, $^3J_{HH}$= 5.4 Hz, H3′), 5.49 (dd, 1H, $^3J_{HH}$= 3.8 Hz, $^3J_{HH}$= 5.8 Hz, H2′), 6.51 (d, 1H, $^3J_{HH}$= 3.7 Hz, H1′), 8.21 (dd, 1H, $^3J_{HH}$= 6.5 Hz, $^3J_{HH}$= 8.7 Hz, H5), 8.92 (d, 1H, $^3J_{HH}$= 8.0 Hz, H4), 9.13 (d, 1H, $^3J_{HH}$= 6.4 Hz, H6), 9.37 (s, 1H, H2). $^{13}$C NMR ($D_2O$), δ, ppm: 19.89 (Me), 19.34 (Me), 20.28 (Me), 20.50 (Me from acetic acid residue), 62.75 (C5′), 69.54 (C3′), 76.48 (C2′), 82.77 (C4′), 97.46 (C1′), 119.75 (CF3, $^1J_{CF}$=316 Hz), 128.78 (C5), 134.33 (C3), 140.55 (C2), 143.20 (C6), 146.36 (C4), 165.49 ($CONH_2$), 172.46 (CO), 172.50 (CO), 173.40 (CO), (CO from acetic acid residue). MS: found m/z = 380.84 (M). HRMS found: 381.12965. Calculated for $C_{17}H_{21}N_2O_8$ (M): 381.12924.

**[(2R,3S,5R)-3,4-Diacetoxy-5-(3-carbamoyl-4H-pyridin-1-yl)tetrahydrofuran-2-yl]methyl acetate (NRH TA, 4a).** In a round bottom flask flushed with nitrogen, compound **3a** (2.85 g, ca. 0.004 mol) was dissolved in a nitrogen-purged DCM (40 mL) and 13 mL of saturated aqueous $NaHCO_3$ solution were added, followed by addition of solid sodium dithionite (ca. 85%; 4.27 g; 0.021 mol) and 7 mL of water at stirring and at room temperature. The biphasic reaction mixture was stirred at room temperature for 4 h, and then brine (30 mL) and DCM (40 mL) were added. Yellow organic phase was separated, washed twice with brine, dried over $Na_2SO_4$, filtered and evaporated under reduced pressure to give light yellow foam (1.35 g; 84% based on compound **4**). $^1$H NMR ($CDCl_3$), δ, ppm: 2.02 (s, 3H, Me), 2.04 (s, 3H, Me), 2.10 (s, 3H, Me), 3.06 (q, 2H, $^3J_{HH}$= 1.4 Hz, H4), 4.11 (dd, 1H, $^3J_{HH}$= 4.7 Hz, $^3J_{HH}$= 3.2 Hz, H4′), 4.20–4.21 (m, 2H, H5′), 4.80 (dt, 1H, $^3J_{HH}$= 3.4 Hz, $^3J_{HH}$= 8.2 Hz, H5), 4.89 (d, 1H, $^3J_{HH}$= 7.0 Hz, H1′), 5.11 (m, 1H, H2′), 5.18 (dd, 1H, $^3J_{HH}$= 2.8 Hz, $^3J_{HH}$= 5.8 Hz, H3′), 5.27 (br s, 2H, $NH_2$), 5.88 (dd, 1H, $^4J_{HH}$= 1.7 Hz, $^3J_{HH}$= 8.2 Hz, H6), 7.09 (s, 1H, H2). $^{13}$C NMR ($CDCl_3$), δ, ppm: 18.47 (Me), 18.59 (Me), 18.79 (Me), 21.22 (C4), 61.60 (C5′), 68.87 and 68.91 (C3′ and C2′), 77.05 (C4′), 91.36 (C1′), 100.38 (C3), 102.49 (C5), 123.07 (C6), 134.36 (C2), 167.52 (two overlapped CO), 167.53 (CO), 168.55 (CO). MS: found m/z = 382.96 (M+1). HRMS found: 383.14530. Calculated for $C_{17}H_{23}N_2O_8$ (M+1): 383.144892.

**1-[(2*R*,3*S*,4*R*,5*R*)-3,4-Dihydroxy-5-(hydroxymethyl)tetrahydrofur-2-yl]-1,4-dihydropyridine-3-carboxamide (NRH, 6a).** A PTFE jar was charged with compound **4a** (0.50 g; 0.0013 mol), anhydrous potassium carbonate (0.0180 g; 0.00013 mol) and methanol (0.3 mL; 0.238 g; 0.0074 mol) were added. The reagents were subjected to ball-milling on a Retsch MM400 miller for 25 min at 25 Hz. The jar was allowed to cool down to room temperature. The content of the jar was dissolved in methanol (2×10 mL) and the yellow solution was transferred into a round bottom flask. Volatiles were removed on a rotary evaporator to dryness to give a yellow foam that was triturated with diethyl ether resulting in a yellow powder. Diethyl ether was removed by decantation and the product was dried under reduced pressure at 34°C. Yield: 0.34 g (ca. 100%). $^1$H NMR ($D_2O$), δ, ppm: 2.98 (q, 2H, $^3J_{HH}$= 1.5 Hz, H4), 3.26 (s, 1.5H, 0.5 MeOH), 3.60 and 3.66 (AB part of ABX system, 2H, $J_{AB}$=12.5 Hz, $J_{BX}$= 4.8 Hz, $J_{AX}$= 3.6 Hz, H5′$_A$ and H5′$_B$), 3.88 (dd, 1H, $^3J_{HH}$= 6.8 Hz, $^3J_{HH}$= 3.5 Hz, H4′), 4.04 (dd, 1H, $^3J_{HH}$= 2.9 Hz, $^3J_{HH}$= 5.6 Hz, H3′), 4.11 (m, 1H, H2′), 4.66 (OH, $NH_2$ overlapped with $D_2O$), 4.79 (d, 1H, $^3J_{HH}$= 7.0 Hz, H1′), 4.90 (dt, 1H, $^3J_{HH}$= 3.4 Hz, $^3J_{HH}$= 8.2 Hz, H5), 6.01 (dd, 1H, $^4J_{HH}$= 1.5 Hz, $^3J_{HH}$= 8.2 Hz, H6), 7.06 (s, 1H, H2). $^{13}$C NMR ($D_2O$), δ, ppm: 22.07 (C4), 49.00 (MeOH), 61.63 (C5′), 70.21 (C3′), 71.11 (C2′), 83.56 (C4′), 95.03 (C1′), 101.08 (C3), 105.20 (C5), 125.37 (C6), 137.80 (C2), 172.96 (CO). MS: found m/z = 257.21 (M+1). HRMS found: 257.11376. Calculated for $C_{11}H_{17}N_2O_5$ (M+1): 257.113198.

**3-Carbamoyl-1-((2*R*,3*R*,4*S*,5*R*)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)pyridin-1-ium trifluoromethanesulfonate (NR OTf, 5a)**. Into a 130 mL pressure tube closed with a septum, evacuated and filled with argon, a solution of crude compound **3a** (2.44 g, ca. 0.004 mol as calculated on N-silylated form of **3a**) in anhydrous methanol (30 mL) was added. The solution was cooled down to -78°C at stirring, and ammonia gas (passed through a tube filled with NaOH) was bubbled into the solution through a long metal needle for ca. 5 min. The reaction solution was additionally stirred at -78°C for 10 min, and, subsequently, the septum was removed, and the tube was immediately closed with a threaded PTFE cap and transferred into a freezer (-20°C) and kept at -20°C for 6 days. The pressure tube was transferred into an ice bath, and, by using a cannula, the content of the tube was transferred into a recovery flask, cooled down in the same ice bath to 0°C. The recovery flask was attached to a rotary evaporator, and ammonia gas was evaporated without any external heating and immersion

in a water bath which resulted in a continuous maintaining of the solution temperature below 0°C. After removal of ammonia, residual methanol was removed at ca. 25°C and an oily residue was kept under high vacuum to give a viscous yellow liquid (2.05 g, ca. 90% as calculated on the basis of a mixture of acetamide and compound **5a**). $^{19}$F NMR ($D_2O$), δ, ppm: -78.81. $^1$H NMR ($D_2O$), δ, ppm: 1.86 (s, 8H, Me of $CH_3CONH_2$), 3.21 (s, 0.8H, Me of $CH_3OH$), 3.78 and 3.93 (AB part of ABX system, 2H, $J_{AB}$=12.9 Hz, $J_{AX}$= 3.5 Hz, $J_{BX}$= 2.9 Hz, H5′$_A$ and H5′$_B$), 4.23 (t, 1H, $^3J_{HH}$= 4.6 Hz, H3′), 4.35–4.36 (m, 1H, H4′), 4.38 (t, 1H, $^3J_{HH}$= 4.8 Hz, H2′), 6.12 (d, 1H, $^3J_{HH}$= 4.4 Hz, H1′), 8.15 (dd, 1H, $^3J_{HH}$= 6.5 Hz, $^3J_{HH}$= 8.7 Hz, H5), 8.85 (d, 1H, $^3J_{HH}$= 8.1 Hz, H4), 9.14 (d, 1H, $^3J_{HH}$= 6.2 Hz, H6), 9.47 (s, 1H, H2). $^{13}$C NMR ($D_2O$), δ, ppm: 21.24 (Me of $CH_3CONH_2$), 48.85 (Me of MeOH), 60.19 (C5′), 69.78 (C3′), 77.44 (C2′), 85.70 (C4′), 99.93 (C1′), 119.60 ($CF_3$, $^1J_{CF}$=315 Hz), 128.38 (C5), 133.94 (C3), 140.35 (C2), 142.60 (C6), 145.62 (C4), 165.69 ($CH_3\underline{C}ONH_2$), 177.32 (CO). MS: found m/z = 254.72 (M). HRMS found: 255.09804. Calculated for $C_{11}H_{15}N_2O_5$ (M): 255.09755.

**Trimethylsilyl nicotinate (2b).** Under an argon atmosphere, nicotinic acid (4.00 g; 0.0325 mol) was added into a 50 mL round-bottom single-neck flask, followed by HMDS (20 mL; 15.73 g; 0.0975 mol; 3 equiv.) and 6–8 small $(NH_4)_2SO_4$ crystals. The reaction mixture was heated in an oil bath to 110°C (oil bath temperature) at stirring. The reaction mixture was allowed to react overnight at ca. 95°C (oil bath temperature). Next day, 20 mL of anhydrous toluene (kept over sodium) were added and the solution was transferred by a syringe, under an argon atmosphere, into a recovery flask. The solution was evaporated under reduced pressure to give a colorless clear liquid (5.84 g, 0.030 mol; 92%), containing less than 5 mol % of nicotinic acid, as indicated by $^1$H NMR. The product was stored at -20°C and used directly in the glycosylation reaction. $^1$H NMR (benzene-$d_6$), δ, ppm: 0.00 (s, 9H, $SiMe_3$), 6.40 (dd, 1H, $^3J_{HH}$= 4.8 Hz, $^3J_{HH}$= 7.8 Hz, H5), 7.77 (dt, 1H, $^3J_{HH}$= 8.0 Hz, $^4J_{HH}$= 1.8 Hz, H4), 8.24 (dd, 1H, $^3J_{HH}$= 4.9 Hz, $^4J_{HH}$= 1.5 Hz, H6), 9.18 (d, 1H, $^4J_{HH}$= 1.4 Hz, H2).

**1-((2R,3R,4R,5R)-3,4-diacetoxy-5-(acetoxymethyl)tetrahydrofuran-2-yl)pyridin-1-ium-3-carboxylate (NAR TA, 3b).** A PTFE jar was charged with 1,2,3,5-tetra-*O*-acetyl-D-β-ribofuranose **1** (0.90 g; 0.0028 mol; 1.1 equiv.) and trimethylsilyl pyridine-3-carboxylate (**2b**) (0.50 g; 0.0026 mol), followed by addition of TMSOTf (0.68 g; 0.0031 mol; 1.2 equiv.). The reagents were subjected to ball-milling on a Retsch MM400 miller for 40 min at 25 Hz. The jar was allowed to cool down to room temperature. The content of the jar was dissolved in DCM (30 mL) and the yellowish solution was transferred into a round bottom flask. Volatiles were removed on a rotary evaporator to dryness to give a yellow foam, that contained the desired product as a triflate salt and ca. 10 mol % of nicotinic acid (after hydrolysis in $D_2O$), as indicated by $^1$H NMR ($D_2O$). The product was dissolved in ca. 40 mL of DCM and the solution was poured onto ice. The mixture was neutralized to pH 6–7 with saturated aqueous $NaHCO_3$ (ca. 4.5 mL), added in portions at stirring with an intermittent pH monitoring by a pH paper. Colorless aqueous phase was separated from the yellowish organic phase. The aqueous phase was evaporated under reduced pressure at less than 40°C to give a white solid product (1.39 g) tat was subjected to C18 reversed phase column chromatography using a Biotage system (UV control, a 120 g C18 column: *l*, 15.5 cm; *d*, 3.8 cm). Elution was started with water resulting in separation of nicotinic acid, $NaHCO_3$ and sodium triflate, and continued with a 10:90 vol % ACN/$H_2O$ mixture resulting in elution of the title compound. Evaporation of the appropriate elutes under reduced pressure at less than 40°C gave a colorless sticky residue, to which acetone (3 mL) was added resulting in transformation of the residue into a snow-white crystalline solid dried under reduced pressure to remove residues of acetone. The purified title compound was prepared in 77% yield (0.75 g; 0.002 mol). $^1$H NMR ($D_2O$), δ, ppm: 2.07 (s, 3H, Me), 2.11 (s, 3H, Me), 2.13 (s, 3H, Me), 4.48–4.50 (m, 2H, H5′), 4.84–4.86 (m, 1H, H4′), 5.44 (apparent t, 1H, $^3J_{HH}$= 5.2 Hz, H3′), 5.52 (apparent t, 1H, $^3J_{HH}$= 4.8 Hz, H2′), 6.53 (d, 1H, $^3J_{HH}$= 4.1 Hz, H1′), 8.15 (t, 1H, $^3J_{HH}$= 7.1 Hz,

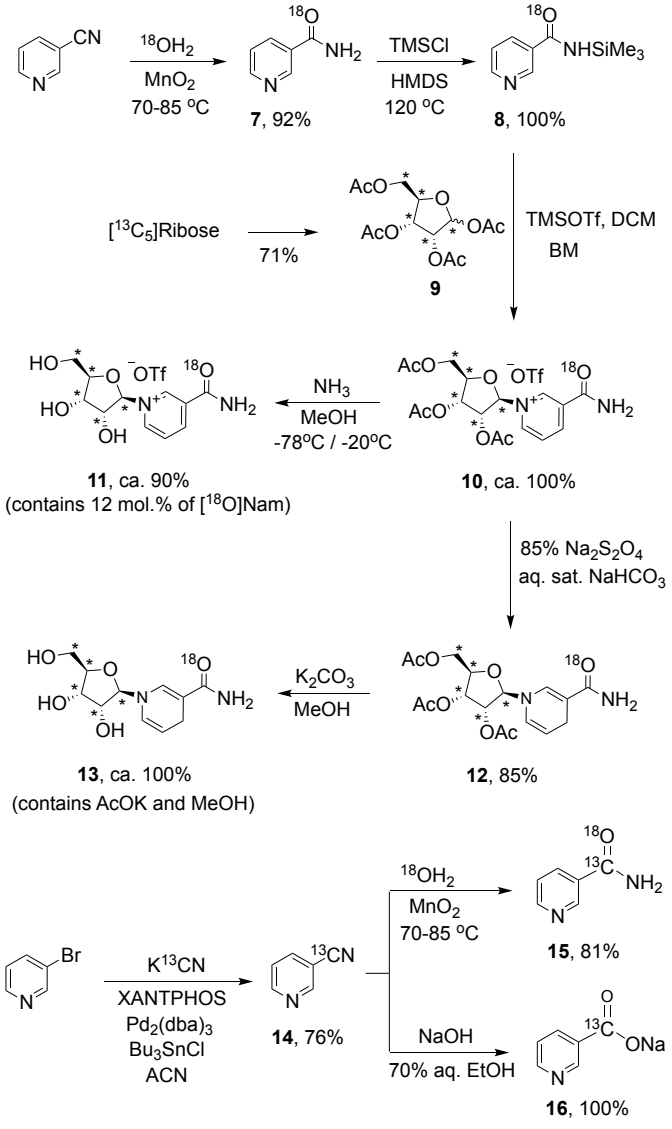
H5), 8.91 (d, 1H, $^3J_{HH}$= 8.0 Hz, H4), 9.04 (d, 1H, $^3J_{HH}$= 6.2 Hz, H6), 9.35 (s, 1H, H2). $^{13}$C NMR ($D_2O$), δ, ppm: 19.76 (Me), 19.84 (Me), 20.17 (Me), 62.74 (C5′), 69.72 (C3′), 76.39 (C2′), 82.61 (C4′), 96.98 (C1′), 128.16 (C5), 137.62 (C3), 140.89 (C2), 141.73 (C6), 147.52 (C4), 167.13 (COO), 172.33 (CO), 172.35 (CO), 173.35 (CO). MS: found m/z = 381.96 (M+1). HRMS found: 382.11357. Calculated for $C_{17}H_{20}NO_9$ (M+1): 382.11326.

**1-((2R,3R,4R,5R)-3,4-diacetoxy-5-(acetoxymethyl)tetrahydrofuran-2-yl)-1,4-dihydropyridine-3-carboxylic acid (NARH TA, 4b).** In a round bottom flask flushed with nitrogen, compound **3b** (0.50 g, 0.0013 mol) was dissolved in water (3 mL). The solution was cooled down in an ice bath, followed by addition of 4 mL of saturated aqueous $NaHCO_3$ solution and solid sodium dithionite (ca. 85%; 0.81 g; 0.0039 mol, 3 equiv.). The reaction solution was stirred at cooling for 3 h 30 min, 0.19 g of 85% sodium dithionite were added and stirring was continued for 20 min. EtOAc (30 mL) was added. Organic phase was separated, aqueous phase was extracted with EtOAc, combined organic phase was dried over $Na_2SO_4$, filtered and evaporated under reduced pressure to give yellowish viscous residue. DCM was added and evaporated under reduced pressure to give yellowish foam that was triturated into yellowish powder (0.38 g; 75%). $^1$H NMR (acetone-$d_6$), δ, ppm: 1.93 (s, 3H, Me), 1.95 (s, 3H, Me), 1.99 (s, 3H, Me), 2.89 (m, 2H, H4), 4.10–4.12 (m, 1H, H4′), 4.14–4.16 (m, 2H, H5′), 4.74 (dt, 1H, $^3J_{HH}$= 3.3 Hz, $^3J_{HH}$= 8.2 Hz, H5), 4.98 (d, 1H, $^3J_{HH}$= 7.0 Hz, H1′), 5.11–5.16 (m, 2H, H2′ and H3′), 5.99 (d, 1H, $^3J_{HH}$= 8.2 Hz, H6), 7.19 (s, 1H, H2). $^{13}$C NMR (acetone-$d_6$), δ, ppm: 19.44 (Me), 19.60 (Me), 19.74 (Me), 22.24 (C4), 63.41 (C5′), 70.56 (C3′), 70.77 (C2′), 78.98 (C4′), 92.93 (C1′), 100.34 (C3), 104.63 (C5), 125.74 (C6), 138.32 (C2), 168.23 (CO), 169.12 (CO), 169.32 (CO), 169.77 (CO). MS: found m/z = 383.93 (M+1). HRMS found: 384.12890. Calculated for $C_{17}H_{22}NO_9$ (M+1): 384.12891.

**1-((2*R*,3*R*,4*S*,5*R*)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)pyridin-1-ium-3-carboxylate (NAR, 5b).** Under an argon atmosphere, in a pressure tube closed with a septum, nicotinic acid riboside triacetate **3b** (1.54 g, 0.004 mol) was dissolved in anhydrous methanol (25 mL) at stirring. The solution was cooled down to -78°C, and anhydrous ammonia gas was passed into the solution for ca. 5 min. The pressure tube was closed with a threaded cap and placed into a freezer at -20°C and kept there for 4 days. The tube was transferred in an ice bath, the threaded cap was removed and replaced by a septum. Using a cannula, the reaction solution in the pressure tube was transferred into a recovery flask, cooled in the same ice bath. Volatiles were removed from the reaction solution on a rotary evaporator without any external heating (which resulted in a continuous maintaining of the solution temperature below 0°C). After removal of ammonia, residual methanol was removed at ca. 20°C and a peach-colored wet solid was suspended in acetone (ca. 5 mL). The mixture was kept in a freezer at -20°C for ca. 30 min, and the solid product was filtered, washed with acetone and dried a desiccator over phosphorus pentoxide to give a peach-colored powder (0.79 g, 77%). $^1$H NMR ($D_2O$), δ, ppm: 3.81 and 3.94 (AB part of ABX system, 2H, $J_{AB}$=12.9 Hz, $J_{AX}$= 3.8 Hz, $J_{BX}$= 2.8 Hz, H5′$_A$ and H5′$_B$), 4.26 (apparent t, 1H, $^3J_{HH}$= 4.5 Hz, H3′), 4.36–4.38 (m, 1H, H4′), 4.40 (apparent t, 1H, $^3J_{HH}$= 4.8 Hz, H2′), 6.12 (d, 1H, $^3J_{HH}$= 4.6 Hz, H1′), 8.09 (t, 1H, $^3J_{HH}$= 7.1 Hz, H5), 8.85 (d, 1H, $^3J_{HH}$= 8.0 Hz, H4), 9.05 (d, 1H, $^3J_{HH}$= 6.2 Hz, H6), 9.36 (s, 1H, H2). $^{13}$C NMR ($D_2O$), δ, ppm: 60.39 (C5′), 69.97 (C3′), 77.42 (C2′), 87.58 (C4′), 99.56 (C1′), 127.91 (C5), 137.26 (C3), 140.87 (C2), 141.31 (C6), 146.85 (C4), 167.54 (CO). MS: found m/z = 255.74 (M+1). HRMS found: 256.08195. Calculated for $C_{11}H_{14}NO_6$ (M+1): 256.08156.

**1-((2*R*,3*R*,4*S*,5*R*)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-1,4-dihydropyridine-3-carboxylic acid (NARH, 6b).** A 25 wt. % solution of MeONa in MeOH (0.52 mL, 0.0023 mol; 1.1 equiv.) was added in one portion to a solution of NARH TA **5b** (0.8 g, 0.0021 mol) in 8 mL of anhydrous MeOH under an argon atmosphere at stirring. After stirring for ca. 30 min, the solution was concentrated under reduced pressure to give NARH sodium salt as a light-orange solid in ca. 100% yield (0.62 g). $^1$H NMR ($D_2O$), δ, ppm: 1.81 (s, 0.6H, Me of $CH_3COONa$), 2.91 (m, 2H, H4), 3.25 (s, 0.34H, Me of $CH_3OH$), 3.59 and 3.65 (AB part of ABX system, 2H, $J_{AB}$=12.4 Hz, $J_{AX}$= 5.0 Hz, $J_{BX}$= 3.7 Hz, H5′$_A$ and H5′$_B$), 3.81–3.84 (m, 1H, H4′), 3.98 (dd, 1H, $J_{HH}$= 3.1 Hz, $^3J_{HH}$= 5.8 Hz, H3′), 4.08 (apparent t, 1H, $^3J_{HH}$= 6.3 Hz, H2′), 4.71 (d, 1H, $^3J_{HH}$= 7.0 Hz, H1′), 4.80 (dt, 1H, $J_{HH}$= 3.6 Hz, $^3J_{HH}$= 8.1 Hz, H5), 5.95 (dd, 1H, $^4J_{HH}$= 1.4 Hz, $^3J_{HH}$= 8.2 Hz, H6), 6.90 (s, 1H, H2). $^{13}$C NMR ($D_2O$), δ, ppm: 23.17 (C4), 23.24 (Me of $CH_3COONa$), 48.84 (Me of $CH_3OH$), 61.69 (C5′), 70.31 (C3′), 70.91 (C2′), 83.22 (C4′), 95.15 (C1′), 104.69 (C5), 105.92 (C3), 126.11 (C6), 136.42 (C2), 177.05 (CO). MS: found m/z = 257.72 (M+1), 320.84 (M+Na+$CH_3CN$). HRMS found: 258.09742. Calculated for $C_{11}H_{16}NO_6$ (M+1): 258.09721.

## Synthesis of stable-isotope labelled analogues




**Scheme 2S.** Chemical syntheses of labelled precursors of $NAD^+$.

**[$^{18}$O]Nicotinamide (7).** Into a pressure tube evacuated and filled with argon, 3-cyanopyridine (1.50 g, 0.0144 mol) was added, followed by manganese oxide (0.134 g; 0.00154) and [$^{18}$O]water (1.00 mL, 0.0475 mol, 3.3 equiv.) added from a syringe under an argon atmosphere. The tube was closed with a threaded PTFE cap, immersed in an oil bath and heated therein at 80°C for 24 hours. Next day, the tube was taken from the bath and allowed to cool down to room temperature. The contents of the tube were dissolved in a mixture of 150 mL of DCM and 150 mL of acetonitrile. The solution was filtered twice through a filter paper and the filtrate was concentrated under reduced pressure to give white solid (1.64 g, 92%). $^1$H NMR ($D_2O$), δ, ppm: 7.48 (dd, 1H, $^3J_{HH}$= 8.0 Hz, $^3J_{HH}$= 5.1 Hz, H5), 8.13 (dt, 1H, $^3J_{HH}$= 8.0 Hz, $^4J_{HH}$= 1.6 Hz, H4), 8.59 (dd, 1H, $^3J_{HH}$= 5.0 Hz, $^4J_{HH}$= 1.0 Hz, H6), 8.81 (d, 1H, $^4J_{HH}$= 1.5 Hz, H2). $^{13}$C NMR ($D_2O$), δ, ppm: 124.17 (C5), 129.26 (C3), 136.47 (C4), 145.53 (C2), 151.71 (C6), 170.63 (CO). MS: found m/z = 124.72 (M+1), 165.72 (M+$CH_3CN$+1). HRMS found: 125.05938. Calculated for $C_6H_7N_2{}^{18}O$ (M+1): 125.05953.

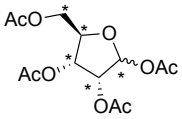
***N*-(trimethylsilyl)-[$^{18}$O]nicotinamide (8).** A mixture of [$^{18}$O]nicotinamide (0.40 g; 0.032 mol), HMDS (5.00 mL) and TMSCl (0.81 mL, 0.70 g, 0.0064 mol) was heated in an oil bath to 110-120°C (oil bath temperature) at intensive stirring. Gas evolution started at ca. 115°C and dissolution completed at ca. 120°C after 3-4 hours of reacting. The reaction solution was left stirred at 105-110°C for ca. 24 hours. Next day, the reaction mixture was allowed to cool down to room temperature and clear colorless solution was transferred into a 25 mL round-bottom single-neck flask under argon through a cannula and evaporated to dryness on a rotary evaporator followed by drying under high vacuum to give a white crystalline product (0.632 g, 100%). $^1$H NMR ($C_6D_6$), δ, ppm: 0.16 (br s, 9H, $SiMe_3$), 5.19 (br s, 1H, NH), 6.54 (ddd, 1H, $^3J_{HH}$= 4.8 Hz, $^3J_{HH}$= 7.9 Hz, $^4J_{HH}$= 0.66 Hz, H5), 7.72 (dt, 1H, $^3J_{HH}$= 8.0 Hz, $^4J_{HH}$= 1.9 Hz, H4), 8.35 (dd, 1H, $^3J_{HH}$= 4.8 Hz, $^4J_{HH}$= 1.7 Hz, H6), 8.82 (d, 1H, $^4J_{HH}$= 2.0 Hz, H2).

**[$^{13}$C-*nitrile*]Nicotinonitrile (14).** An argon-purged pressure tube was charged with $^{13}$C-KCN (1.00 g, 0.015 mol), anhydrous acetonitrile (8 mL) and 3-bromopyridine (1.74 g, 0.011 mol). The tube was evacuated and purged with argon. Tributyltin chloride (1.17 mL, 0.061 mol), XANTPHOS (62 mg, 0.11 mmol) and $Pd_2(dba)_3$ (103 mg, 0.11 mmol) were subsequently added into the pressure tube. The tube was evacuated and filled with argon, closed with a threaded PTFE cap. The reaction mixture in the tube was first stirred at room temperature for 30–35 min, then it was heated in an oil bath at 90–98°C (oil bath temperature) for ca. 19 hours. Next day, after completion of the reaction (confirmed by $^1$H NMR spectroscopy), the reaction mixture in the tube was diluted with DCM (50 mL), the solution was filtered and evaporated under reduced pressure. The residue was purified by a silica gel column chromatography (column: *l*, 20 cm; *d*, 1.5 cm; eluent: 3:7 hexanes/EtOAc mixture). Fractions containing the desired product were combined and evaporated to dryness to give a yellowish crystalline product (0.88 g, 76%). $^1$H NMR ($CDCl_3$), δ, ppm: 7.43 (dd, 1H, $^3J_{HH}$= 8.0 Hz, $^3J_{HH}$= 5.0 Hz, H5), 7.96 (ddt, 1H, $^3J_{HC}$= 7.8 Hz, $^3J_{HH}$= 5.5 Hz, $^4J_{HH}$= 1.9 Hz, H4), 8.77 (dt, 1H, $^3J_{HH}$= 5.0 Hz, $^4J_{HH}$= 1.2 Hz, H6), 8.84 (apparent t, 1H, J= 2.3 Hz, H2). $^{13}$C NMR ($CDCl_3$), δ, ppm: 110.11 (d, $^1J_{CC}$=84 Hz, C3), 116.47 (CN), 123.61 (d, $^3J_{CC}$=4.5 Hz, C5), 139.22 (d, $^2J_{CC}$=1.8 Hz, C4), 152.48 (d, $^2J_{CC}$=3.6 Hz, C2), 152.99 (C6). MS: found m/z = 105.84 (M+1), 147.11 (M+$CH_3CN$+1). HRMS found: 106.04786. Calculated for $^{13}C^{12}C_5H_5N_2$ (M+1): 106.04808.

**[$^{18}$O,$^{13}$C-*carbonyl*]Nicotinamide (15).** Into a pressure tube (*l*, 20 cm; *d*, 0.8 cm) evacuated and filled with argon, [$^{13}$C-*nitrile*]nicotinonitrile (0.45 g, 0.0043 mol) was added, followed by manganese oxide (0.05 g; 0.6 mmol) and [$^{18}$O]water (0.30 mL, 0.015 mol, 3.5 equiv.) added from a syringe under an argon atmosphere. The tube was closed with a threaded PTFE cap, immersed in an oil bath and heated therein at 70–85°C overnight. Next day, the tube was taken from the bath and allowed to cool down to room temperature. The contents of the tube were dissolved in a

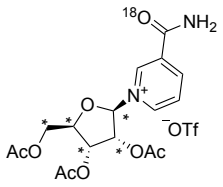
DCM/acetonitrile mixture. The solution was filtered twice through a filter paper and the filtrate was concentrated under reduced pressure to give white solid (0.44 g, 81%). $^{1}$H NMR ($D_2O$), δ, ppm: 7.48 (dd, 1H, $^{3}J_{HH}$= 8.0 Hz, $^{3}J_{HH}$= 5.1 Hz, H5), 8.13 (dddd, 1H, $^{3}J_{HC}$= 8.0 Hz, $^{3}J_{HH}$= 3.9 Hz, $^{4}J_{HH}$= 2.2 Hz, $^{4}J_{HH}$= 1.9 Hz, H4), 8.60 (apparent d, 1H, $^{3}J_{HH}$= 4.5 Hz, H6), 8.82 (br s, 1H, H2). $^{13}$C NMR ($D_2O$), δ, ppm: 124.16 (d, $^{3}J_{CC}$=3.5 Hz, C5), 129.27 (d, $^{1}J_{CC}$=64 Hz, C3), 136.42 ($^{2}J_{CC}$=2.1 Hz, C4), 147.61 (d, $^{2}J_{CC}$=3.6 Hz, C2), 151.79 (C6), 170.74 (CO). MS: found m/z = 126.05 (M+1), 167.08 (M+$CH_3CN$+1). HRMS found: 126.06273. Calculated for $^{13}C^{12}C_5H_7N_2{}^{18}O$ (M+1): 126.06289.

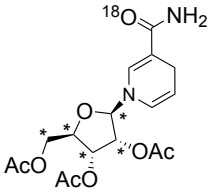
**[$^{13}$C-*carbonyl*]Nicotinic acid, sodium salt (16).** In a 25 mL single-neck flask, sodium hydroxide (0.39 g, 0.0097 mol) was dissolved in a mixture of 2.8 mL of ethanol and 1.2 mL of water. To this solution, [$^{13}$C-*nitrile*]nicotinonitrile (0.35 g, 0.0033 mol) was added and the reaction mixture was heated in an oil-bath under reflux (oil bath temperature was ca. 85°C) for 3.5 hours. The reaction solution was allowed to cool down to room temperature and neutralized with 8 mL of 1 M HCl to pH in the range of 5–6. Volatiles were removed under vacuum. The solid residue was subjected to a column chromatography on silica gel to remove inorganic salts (eluted with methanol). Elutes were combined and evaporated to give a white powder of sodium nicotinate (0.49 g, 100%). $^{1}$H NMR ($D_2O$), δ, ppm: 7.43 (dd, 1H, $^{3}J_{HH}$= 8.0 Hz, $^{3}J_{HH}$= 5.1 Hz, H5), 8.16 (dddd, 1H, $^{3}J_{HC}$= 7.8 Hz, $^{3}J_{HH}$= 3.8 Hz, $^{4}J_{HH}$= 2.2 Hz, $^{4}J_{HH}$= 1.8 Hz, H4), 8.51 (dd, 1H, $^{3}J_{HH}$= 5.0 Hz, $^{4}J_{HH}$= 1.2 Hz, H6), 8.84 (br s, 1H, H2). $^{13}$C NMR ($D_2O$), δ, ppm: 123.95 (d, $^{3}J_{CC}$=3.6 Hz, C5), 132.39 (d, $^{1}J_{CC}$=66 Hz, C3), 137.80 ($^{2}J_{CC}$=1.5 Hz, C4), 148.85 (d, $^{2}J_{CC}$=3.7 Hz, C2), 150.23 (C6), 173.19 (CO). MS: found m/z = 124.64 (M+1), 165.66 (M+$CH_3CN$+1). HRMS found: 125.04246. Calculated for $^{13}C^{12}C_5H_6NO_2$ (M+1): 125.04266.

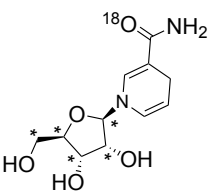



**1,2,3,5-Tetra-*O*-acetyl-α/β-D-[$^{13}C_5$]ribofuranose ([$^{13}C_5$]RTA, 9).** [$^{13}C_5$]Ribose (1.00 g, 0.0064 mol) was dissolved in anhydrous methanol (16 mL). The solution was cooled down in an ice bath at stirring and 98% sulfuric acid (0.08 mL) was added to the solution. The reaction solution was kept at ca. 0°C overnight. Next day, dry pyridine (3.2 mL) was added, and the volatiles were evaporated under vacuum. Another portion of dry pyridine (5 mL) was added and evaporation was repeated. A syrupy residue was dissolved in dry pyridine (8 mL), cooled on ice, and acetic anhydride (3.12 mL) was added thereto with periodical shaking. The reaction solution was kept at room temperature for 2 days. Volatiles were evaporated under reduced pressure, the residue was treated with saturated $NaHCO_3$ solution and extracted with DCM. Organic phase was separated, dried over sodium sulfate and filtered. Evaporation of volatiles gave methyl 2,3,5-tri-*O*-acetyl-α/β-D-[$^{13}C_5$]ribofuranoside (1.47 g, 77%) as colorless oil. The crude product (1.40 g, 0.0047 mol) was dissolved in glacial acetic acid (9 mL), acetic anhydride (2.2 mL) was added, and the solution was cooled down in an ice bath at stirring, followed by addition of 98% sulfuric acid (0.5 mL). The cooling bath was removed and stirring was continued at room temperature overnight. The reaction mixture was poured on ice, chloroform and saturated $NaHCO_3$ solution were added. Organic phase was separated, aqueous phase was extracted with chloroform (5 × 20 mL) and diethyl ether (1 × 20 mL). Combined organic phase was dried over $Na_2SO_4$, filtered and evaporated to give 1,2,3,5-tetra-*O*-acetyl-α/β-D-[$^{13}C_5$]ribofuranose as a viscous liquid (1.48 g, 71% as calculated on [$^{13}C_5$]ribose) transformed into a mixture of oil and crystals when being kept at -20°C. According to the 1H NMR, the compound is a mixture of α/β-anomers present in a molar ratio of 0.34:1. $^{1}$H NMR ($CDCl_3$), δ, ppm: 1.97–2.08 (m, 12H, 4×OAc), 3.86–4.34 (dm, 1H, $^{1}J_{CH}$=148.2 Hz, H4), 4.03–4.34 (dm, 2H, $^{1}J_{CH}$=148.2 Hz, H5), 4.97–5.48 (dm, 2H, $^{1}J_{CH}$=158 Hz, H3 and H2), 6.09 (dm, 0.75H, $^{1}J_{CH}$=182.5 Hz, β-H1), 6.35 (dm, 0.25H, $^{1}J_{CH}$=182.5 Hz, J=3.9 Hz α-H1). $^{13}$C NMR ($CDCl_3$), δ, ppm: 20.26–20.98 (m, Me of Ac), 63.25 (d, $^{1}J_{CC}$= 43.3 Hz, α-C5), 63.91 (d, $^{1}J_{CC}$= 43.5 Hz, β-C5), 68.36–70.00 (m, α-C2 and α-C3), 70.47 (t, $^{1}J_{CC}$= 40.0 Hz, β-C3), 74.09 (dd, $^{1}J_{CC}$= 47.3 Hz, $^{1}J_{CC}$= 38.3 Hz, β-C2), 79.25 (dd, $^{1}J_{CC}$= 43.3 Hz, $^{1}J_{CC}$= 40.5 Hz, β-C4), 81.14–81.99 (m, $^{1}J_{CC}$= 42.3 Hz,

α-C4), 93.43–94.61 (m, $^{1}J_{CC}$= 44.8 Hz, α-C1), 98.15 (dd, $^{1}J_{CC}$= 47.4 Hz, J= 3.1 Hz, β-C1), 168.93–170.43 (m, CO of Ac). MS: found m/z: 263.15 ([M–OAc]$^{+}$), 345.13 ([M+Na]$^{+}$), 386.71 ([M+Na+$CH_3CN$]$^{+}$). HRMS found: 346.10136. Calculated for $^{13}C_5{}^{12}C_8H_{18}O_9Na$ (M+Na): 346.10108.

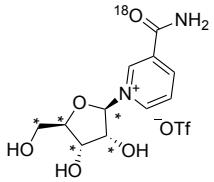
**[$^{13}C_5$,$^{18}$O]-3-Carbamoyl-1-((2R,3R,4R,5R)-3,4-diacetoxy-5-(acetoxymethyl)tetrahydrofuran-2-yl)pyridin-1-ium trifluoromethanesulfonate ([$^{13}C_5$,$^{18}$O]NRTA OTf, 10).** 
A PTFE jar was charged with silylated [$^{18}$O]nicotinamide (0.314 g; 0.0016 mol), 1,2,3,5-tetra-*O*-acetyl-α/β-D-[$^{13}C_5$]ribofuranose (0.562 g; 0.0017 mol), anhydrous DCM (75 μL) and TMSOTf (0.464 g; 0.0021 mol; 1.2 equiv.). The reagents were subjected to ball-milling on a Retsch MM400 miller for 30 min at 30 Hz. The jar was allowed to cool down to room temperature. The content of the jar was dissolved in DCM (2×10 mL) and the yellow solution was transferred into a round bottom flask. Volatiles were removed on a rotary evaporator to dryness to give a yellow foam (1.00 g; quantitative yield) which was used on the next step without additional purification. $^{1}$H NMR ($D_2O$), δ, ppm: 1.95 (Me from acetic acid residue), 2.02 (s, 3H, Me), 2.05 (s, 3H, Me), 2.09 (s, 3H, Me), 4.27 (br s, 1H, 1/2H5′), 4.63 (br s, 0.5H, 1/2H4′, and 1H, 1/2H5′, overlapped with water protons in $D_2O$), 5.01 (s, 0.5H, 1/2H4′), 5.38 (d, 1H, $^{1}J_{CH}$= 158.5 Hz, H3′), 5.50 (d, 1H, $^{1}J_{CH}$= 160.8 Hz, H2′), 6.51 (d, 1H, $^{1}J_{CH}$= 180.4 Hz, H1′), 8.20 (apparent t, 1H, $^{3}J_{HH}$= 7.1 Hz, H5), 8.92 (d, 1H, $^{3}J_{HH}$= 8.1 Hz, H4), 9.13 (br s, 1H, H6), 9.37 (br s, 1H, H2). MS: found m/z = 387.96 (M+1).

**[$^{13}C_5$,$^{18}$O]-[(2R,3S,5R)-3,4-Diacetoxy-5-(3-carbamoyl-4H-pyridin-1-yl)tetrahydrofuran-2-yl]methyl acetate ([$^{13}C_5$,$^{18}$O]NRH TA, 12).** 
In a round bottom flask flushed with nitrogen, [$^{13}C_5$,$^{18}$O]-NR TA OTf (0.45 g, 0.7 mmol) was dissolved in water (2 mL), and a solution of sodium dithionite (0.78 g, ca. 85%, 3.8 mmol) in saturated aqueous $NaHCO_3$ solution (3 mL) was added thereto under cooling in an ice bath and at stirring. The reaction mixture was stirred on ice for ca. 30 min, followed by stirring at room temperature for ca. 2 hours. An additional portion of sodium dithionite (0.10 g, ca. 85%) was added, stirring was continued for ca. 30 min, followed by addition of argon-purged DCM (30 mL). Organic phase was separated, aqueous phase was extracted with DCM several times. Combined organic phase was dried over $Na_2SO_4$, filtered and evaporated under reduced pressure to give light-yellow solid foam (0.245 g, 85%). $^{1}$H NMR ($CD_3OD$), δ, ppm: 1.97 (s, 3H, Me), 2.00 (s, 3H, Me), 2.04 (s, 3H, Me), 2.97 (br s, 2H, H4), 4.12 (dm, 1H, $^{1}J_{CH}$= 151.7 Hz, H4′), 4.17 (dm, 1H, $^{1}J_{CH}$= 148.6 Hz, 2H, H5′), 4.77–4.79 (m, 1H, H5 overlapped with $H_2O$ in $CD_3OD$), 4.90–5.46 (m, 3H, H1′, H2′, H3′), 5.95 (d, 1H, $^{3}J_{HH}$= 8.2 Hz, H6), 7.06 (br s, 1H, H2). MS: found m/z = 390.10 (M+1).

**[$^{13}C_5$,$^{18}$O]-1-[(2*R*,3*S*,4*R*,5*R*)-3,4-Dihydroxy-5-(hydroxymethyl)tetrahydrofur-2-yl]-1,4-dihydropyridine-3-carboxamide ([$^{13}C_5$,$^{18}$O]NRH, 13).** 
A 1.5 mL stainless steel jar was charged with [$^{13}C_5$,$^{18}$O]-NRH TA (0.20 g; 0.5 mmol), followed by addition of anhydrous potassium carbonate (0.041 g; 0.3 mmol) and methanol (0.100 mL; 0.079 g; 2.5 mmol). The reagents were subjected to ball-milling on a Retsch MM400 miller for 30 min at 25 Hz. The jar was allowed to cool down to room temperature. The content of the jar was dissolved in methanol (2×10 mL) and the yellow solution was filtered through a small cotton ball and transferred into a round bottom flask. Volatiles were removed on a rotary evaporator to dryness to give a yellow solid foam as a mixture of the desired [$^{13}C_5$,$^{18}$O]-NRH, potassium acetate and methanol (0.154 g, ca. 100%). According to integration of peaks in $^{1}$H NMR spectrum, the product contained ca. 33 mol % of AcOK and ca. 66 mol % of MeOH. $^{1}$H NMR ($D_2O$), δ, ppm: 1.82 (1H, Me of 0.33 AcOK), 2.98 (br s, 2H, H4), 3.26 (s, 2H, 0.66 MeOH), 3.41–4.31 (m, 5H, H5′$_A$, H5′$_B$, H4′,

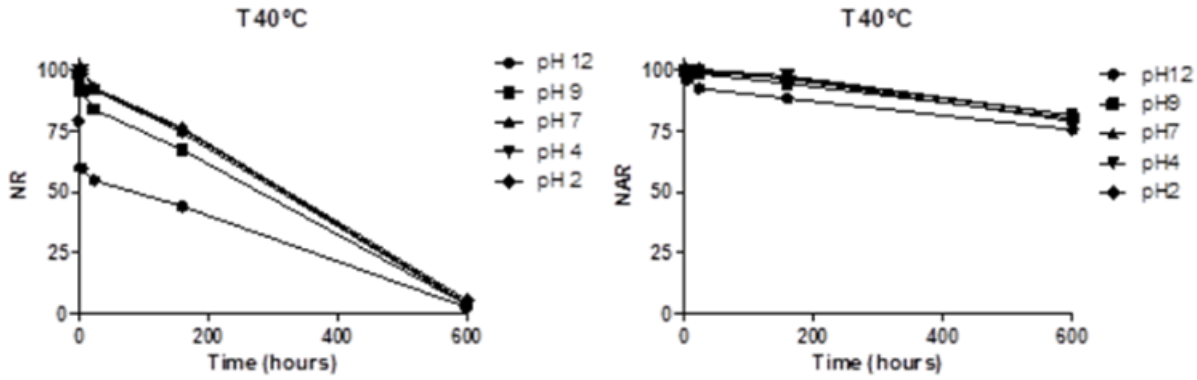
H3′, H2′), 4.66 (OH, $NH_2$ overlapped with $D_2O$), 4.79 (dd, 1H, $^1J_{CH}$= 158.8 Hz, $^3J_{HH}$= 6.7 Hz, H1′), 4.89–4.91 (m, 1H, H5), 6.01 (d, 1H, $^3J_{HH}$= 7.8 Hz, H6), 7.06 (s, 1H, H2). $^{13}$C NMR ($D_2O$), δ, ppm: 21.91 (C4), 23.22 (Me of AcOK), 48.83 (MeOH), 61.45 (d, $^1J_{CC}$= 41.5 Hz, C5′), 69.64–71.33 (m, $^1J_{CC}$= 39 Hz, C3′ and C2′), 83.48 (dm, $^1J_{CC}$= 38.7 Hz, C4′), 94.82 (dd, $^1J_{CC}$= 42.0 Hz, J= 5.7 Hz, C1′), 100.93 (C3), 105.13 (C5), 125.20 (C6), 137.75 (C2), 171.01 (CO of AcOK), 172.96 (CO). MS: found m/z = 264.13 (M+1). HRMS found: 264.13457. Calculated for $^{13}C_5{}^{12}C_6H_{17}N_2{}^{18}OO_4$ (M+1): 264.13422.

**[$^{13}C_5$,$^{18}$O]-3-Carbamoyl-1-((2*R*,3*R*,4*S*,5*R*)-3,4-dihydroxy-5-(hydroxymethyl)-tetrahydrofuran-2-yl)pyridin-1-ium trifluoromethanesulfonate ([$^{13}C_5$,$^{18}$O]NR OTf, 11).** Into




a pressure tube closed with a septum, evacuated and filled with argon, [$^{13}C_5$,$^{18}$O]-NR TA OTf (0.542 g, ca. 0.90 mmol as calculated on N-silylated form of [$^{13}C_5$,$^{18}$O]-NR TA OTf) was dissolved in anhydrous methanol (4 mL). The solution was cooled down to -78°C at stirring, and ammonia gas (passed through a tube filled with NaOH) was bubbled into the solution through a long metal needle for ca. 5 min. The reaction solution was additionally stirred at -78°C for 10 min, and, subsequently, the septum was removed, and the tube was immediately closed with a threaded PTFE cap and transferred into a freezer (-20°C) and kept at -20°C for 6 days. The pressure tube was transferred into an ice bath, and, by using a cannula, the content of the tube was transferred into a recovery flask, cooled down in the same ice bath to 0°C. The recovery flask was attached to a rotary evaporator, and ammonia gas was evaporated without any external heating and immersion in a water bath which resulted in a continuous maintaining of the solution temperature below 0°C. After removal of ammonia, residual methanol was removed at ca. 25°C and an oily residue was kept under high vacuum to give a viscous yellow liquid (0.450 g, ca. 90% as calculated on the basis of a mixture of acetamide, [$^{18}$O]Nam and the desired compound). According to the $^1$H NMR data, the product contained admixture of acetamide, methanol and ca. 12 mol % of [$^{18}$O]Nam. $^{19}$F NMR ($D_2O$), δ, ppm: -78.82. $^1$H NMR ($D_2O$), δ, ppm: 1.90 (s, 6.8H, Me of $CH_3CONH_2$), 3.26 (s, 2.1H, Me of $CH_3OH$), 3.81 and 3.96 (AB part of ABX system, 2H, $^1J_{CH}$= 142.1 Hz, H5′$_A$ and H5′$_B$), 4.27 (dt, 1H, $^1J_{CH}$= 151.3 Hz, $^3J_{HH}$= 3.5 Hz, H3′), 4.19–4.63 (dm, 2H, $^1J_{CH}$= 151.5 Hz, H4′ and H2′), 6.16 (d, 1H, $^1J_{CH}$= 177.1 Hz, H1′), 8.19 (dd, 1H, $^3J_{HH}$= 6.5 Hz, $^3J_{HH}$= 7.8 Hz, H5), 8.89 (d, 1H, $^3J_{HH}$= 8.1 Hz, H4), 9.17–9.20 (m, 1H, H6), 9.52 (s, 1H, H2). $^{13}$C NMR ($D_2O$), δ, ppm: 21.23 (Me of $CH_3CONH_2$), 48.84 (Me of MeOH), 60.16 (d, $^1J_{CC}$= 40.4 Hz, C5′), 69.75 (dt, $^1J_{CC}$= 37.6 Hz, J= 3.4 Hz, C3′), 77.42 (t, $^1J_{CC}$= 38.5 Hz, C2′), 87.67 (t, $^1J_{CC}$= 39.9 Hz, C4′), 99.91 (dd, $^1J_{CC}$= 40.0 Hz, J= 3.2 Hz, C1′), 119.60 ($CF_3$, $^1J_{CF}$=315 Hz), 128.37 (C5), 133.96 (C3), 140.36 (C2), 142.61 (C6), 145.63 (C4), 165.73 ($CH_3\underline{C}ONH_2$), 177.35 (CO). MS: found m/z = 261.26 (M+1). HRMS found: 262.11893. Calculated for $^{13}C_5{}^{12}C_6H_{15}N_2{}^{18}OO_4$ (M+1): 262.11857.

**Study of stability of NRCl and NAR in aqueous solutions.** 500 µL of NMR samples containing a 0.5 mM solution of NR chloride and a 0.5 mM solution of NAR prepared in $D_2O$ at an initial pH 4, 7, 9, 12 were kept for a period of 4 weeks at 40ºC. At regular intervals, $^1$H-NMR spectra for these samples were acquired on a Bruker Avance 400 NMR instrument (400MHz). The data were processed offline using TopSpin™ software (Bruker). The intensity of the anomeric H-1 hydrogen peak of NR and the intensity of the H-6 hydrogens of (NR and Nam) were measured. Similarly, the intensity of the anomeric H-1 hydrogen peak of NAR and the intensity of the H-6 hydrogens of (NAR and NA) were measured. % changes in the ratio were plotted as a function of time.




**Graph 1**: (a) Stability of NR (chloride salt form) and (b) NAR in $D_2O$ as measured by $^1H$ NMR overtime.

**Literature references:**

[1] WO 2015/014722
[2] N. Zhang, A. A. Sauve, *Curr Protoc Nucleic Acid Chem*, 2017, **71**, 14.14.1–14.14.9.
[3] WO 2016/149395
[4] WO 2018/089830
[5] C. Yang, J. M. Williams, *Org Lett*, 2004, **6**, 2837–2840.
[6] C. Battilocchio, J. M. Hawkins, S. V. Ley, *Org. Lett,* 2014, **16**, 1060–1063.
[7] R. D. Guthrie, S. C. Smith, *Biochem Prep*, 1971, **13**, 1–3.
[8] B. L. Kam, J.-L. Barascut, J.-L. Imbach, *Carbohydr Res,* 1979, **69**, 135–142.

**Table 1S.** Isotopic incorporation according to HRMS measurements.

| **Compound name** | **Relative percentage of isotopologues from HRMS measurements** | | | | | | | | | **Isotopic incorporation, %** |
|---|---|---|---|---|---|---|---|---|---|---|
| | MW+0† | MW+1 | MW+2 | MW+3 | MW+4 | MW+5 | MW+6 | MW+7 | MW+8 | |
| [$^{18}$O]Nicotinamide (**7**) | 2.0% | | 100.0% | 6.1%* | | | | | | 98% |
| [$^{13}$C-*nitrile*]Nicotinonitrile (**14**) | | 100.0% | 4.6%* | | | | | | | 100% |
| [$^{18}$O,$^{13}$C-*carbonyl*]Nicotinamide (**15**) | | 2.6% | | 100.0% | 5.0%* | | | | | 97% |
| [$^{13}$C-*carbonyl*]Nicotinic acid, sodium salt (**16**) | | 100.0% | 5.1%* | | | | | | | 100% |
| 1,2,3,5-Tetra-*O*-acetyl-a/b-d-[$^{13}C_5$]ribofuranose (**9**) | | | | | 4.4% | 100.0% | 8.1%* | | | 96% |
| [$^{13}C_5$,$^{18}$O]-1-[(2*R*,3*S*,4*R*,5*R*)-3,4-Dihydroxy-5-(hydroxymethyl)tetrahydrofur-2-yl]-1,4-dihydropyridine-3-carboxamide (**13**) | | | | | | 1.9% | 4.3% | 100.0% | 5.8%* | 94.5% |
| [$^{13}C_5$,$^{18}$O]-3-Carbamoyl-1-((2*R*,3*R*,4*S*,5*R*)-3,4-dihydroxy-5-(hydroxymethyl)-tetrahydrofuran-2-yl)pyridin-1-ium trifluoromethanesulfonate (**11**) | | | | | | 1.5% | 4.0% | 100.0% | 5.7%* | 95% |

**Notices:**
* Natural abundance
† MW+0 stands for non-labelled isotopologue

**Table 2S.** $^{1}$H NMR data of synthesized compounds.

| Compound (Solvent) | Chemical shifts, multiplicity of peaks (J values in Hz) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | H2 | H4 | H5 | H6 | H1’ | H2’ | H3’ | H4’ | H5’ |
| **2a** ($CDCl_3$) | 8.95, d (J = 2.2) | 8.09, dt (J = 2.0; 7.9) | 7.32, dd (J = 4.8; 8.0) | 8.66, dd (J = 1.6; 4.9) | | | | | |
| **7** ($D_2O$) | 8.81, d (J = 1.5) | 8.13, dt (J = 1.6; 8.0) | 7.48, dd (J = 5.1; 8.0) | 8.59, dd (J = 1.0; 5.0) | | | | | |
| **8** ($C_6D_6$) | 8.82, d (J = 2.0) | 7.72, dt (J = 1.9; 8.0) | 6.54, ddd (J = 0.7; 4.8; 7.9) | 8.35, dd (J = 1.7; 4.8) | | | | | |
| **14** ($CDCl_3$) | 8.84, t (J = 2.3) | 8.09, ddt (J = 1.9; 5.5; 7.8) | 7.43, dd (J = 5.0; 8.0) | 8.77, dt (J = 1.2; 5.0) | | | | | |
| **15** ($D_2O$) | 8.82, br s | 8.13, dddd (J = 1.9; 2.2; 3.9; 8.0) | 7.48, dd (J = 5.1; 8.0) | 8.60, d (J = 4.5) | | | | | |
| **16** ($D_2O$) | 8.84, br s | 8.16, dddd (J = 1.8; 2.2; 3.8; 7.8) | 7.43, dd (J = 5.1; 8.0) | 8.51, dd (J = 1.2; 5.0) | | | | | |
| **2b** ($C_6D_6$) | 9.18, d (J = 1.4) | 7.77, dt (J = 1.8; 8.0) | 6.40, dd (J = 4.8; 7.8) | 8.24, dd (J = 1.5; 4.9) | | | | | |
| **3a** ($D_2O$) | 9.37, s | 8.92, d (J = 8.0) | 8.21, dd (J = 6.5; 8.7) | 9.13, d (J = 6.4) | 6.51, d (J = 3.7) | 5.49, dd (J = 3.8; 5.8) | 5.38, t (J = 5.4) | 4.80–4.83, m | 4.42–4.50, m |
| **10** ($D_2O$) | 9.37, br s | 8.92, d (J = 8.1) | 8.20, t (J = 7.1) | 9.13, br s | 6.51, d ($^{1}J_{CH}$ = 180) | 5.50, d ($^{1}J_{CH}$ = 161) | 5.38, d ($^{1}J_{CH}$ = 158) | 4.27–5.01, m | |
| **4a** ($CDCl_3$) | 7.09, s | 3.06, q (J = 1.4) | 4.80, dt (J = 3.4; 8.2) | 5.88, dd (J = 1.7; 8.2) | 4.89, d (J = 7.0) | 5.10–5.13, m | 5.18, dd (J = 2.8; 5.8) | 4.11, dd (J = 3.2; 4.7) | 4.20–4.21, m |
| **12** ($CD_3OD$) | 7.06, br s | 2.97, br s | 4.77–4.79, m | 5.95, d (J = 8.2) | 4.90–5.46, m | | | 4.12, dm ($^{1}J_{CH}$ = 152) | 4.17, dm ($^{1}J_{CH}$ = 149) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **6a** ($D_2O$) | 7.06, s | 2.98, q (J = 1.5) | 4.90, dt (J = 3.4; 8.2) | 6.01, dd (J = 1.5; 8.2) | 4.79, d (J = 7.0) | 4.09–4.12, m | 4.04, dd (J = 2.9; 5.6) | 3.88, dd (J = 3.5; 6.8) | 3.60, 3.66, AB of ABX (J =12.5; 3.6; 4.8) |
| **13** ($D_2O$) | 7.06, s | 2.98, br s | 4.89–4.91, m | 6.01, d (J = 7.8) | 4.79, dd (J = 6.7; $^1J_{CH}$ = 159) | 3.41–4.31, m | | | |
| **5a** ($D_2O$) | 9.47, s | 8.85, d (J = 8.1) | 8.15, dd (J = 6.5; 8.7) | 9.14, d (J = 6.2) | 6.12, d (J = 4.4) | 4.38, t (J = 4.8) | 4.23, t (J = 4.6) | 4.35–4.36, m | 3.78, 3.93, AB of ABX (J = 12.9; 2.9; 3.5) |
| **11** ($D_2O$) | 9.52, s | 8.89, d (J = 8.1) | 8.19, dd (J = 6.5;7.8) | 9.17–9.20, m | 6.16, d ($^1J_{CH}$ = 177) | 4.19–4.63, dm ($^1J_{CH}$ = 151) | 4.27, dt ($^1J_{CH}$ = 151; J = 3.6) | 4.19–4.63, dm ($^1J_{CH}$ = 151) | 3.81, 3.96, AB of ABX ($^1J_{CH}$ = 142) |
| **3b** ($D_2O$) | 9.35, s | 8.91, d (J = 8.0) | 8.15, t (J = 7.1) | 9.04, d (J = 6.2) | 6.53, d (J = 4.1) | 5.52, t (J = 4.8) | 5.44, t (J = 5.2) | 4.84–4.86, m | 4.48–4.50, m |
| **4b** (acetone-$d_6$) | 7.19, s | 2.89, m | 4.74, dt (J = 3.3; 8.2) | 5.99, d (J = 8.2) | 4.98, d (J = 7.0) | 5.11–5.16, m | | 4.10–4.12, m | 4.14–4.16, m |
| **5b** ($D_2O$) | 9.36, s | 8.85, d (J = 8.0) | 8.09, t (J = 7.1) | 9.05, d (J = 6.2) | 6.12, d (J = 4.6) | 4.40, t (J = 4.8) | 4.26, t (J = 4.5) | 4.36–4.38, m | 3.81, 3.94, AB of ABX (J = 12.9; 2.8; 3.8) |
| **6b** ($D_2O$) | 6.90, s | 2.91, m | 4.80, dt (J = 3.6; 8.1) | 5.95, dd (J = 1.4; 8.2) | 4.71, d (J = 7.0) | 4.08, t (J = 6.3) | 3.98, dd (J = 3.1; 5.8) | 3.81–3.84, m | 3.59, 3.65, AB of ABX (J =12.4; 3.7; 5.0) |
| **9** ($CDCl_3$) | | | | | 6.09 (β), 6.35 (α), dm ($^1J_{CH}$ = 181) | 4.97–5.48, dm ($^1J_{CH}$ = 158) | | 3.86–4.34, dm ($^1J_{CH}$ = 148) | 4.04–4.34, dm ($^1J_{CH}$ = 148) |

**Table 3S.** $^{13}C$ NMR data of synthesized compounds.

| Compound (Solvent) | Chemical shifts, multiplicity of peaks (J values in Hz) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | C2 | C3 | C4 | C5 | C6 | C1' | C2' | C3' | C4' | C5' |
| **2a** ($CDCl_3$) | 149.05 | 131.31 | 135.99 | 124.09 | 153.00 | | | | | |
| **7** ($D_2O$) | 145.53 | 129.26 | 136.47 | 124.17 | 151.71 | | | | | |
| **14** ($CDCl_3$) | 152.48, d ($^2J_{CC}$ = 3.6) | 110.11, d ($^1J_{CC}$ = 84) | 139.22, d ($^2J_{CC}$ = 1.8) | 123.61, d ($^3J_{CC}$ = 4.5) | 152.99 | | | | | |
| **15** ($D_2O$) | 147.61, d ($^2J_{CC}$ = 3.6) | 129.27, d ($^1J_{CC}$ = 64) | 136.42, d ($^2J_{CC}$ = 2.1) | 124.16, d ($^3J_{CC}$ = 3.5) | 151.79 | | | | | |
| **16** ($D_2O$) | 148.85, d ($^2J_{CC}$ = 3.7) | 132.39, d ($^1J_{CC}$ = 66) | 137.80, d ($^2J_{CC}$ = 1.5) | 123.95, d ($^3J_{CC}$ = 3.6) | 150.23 | | | | | |
| **3a** ($D_2O$) | 140.55 | 134.33 | 146.36 | 128.78 | 143.20 | 97.46 | 76.48 | 69.54 | 82.77 | 62.75 |
| **4a** ($CDCl_3$) | 134.36 | 100.38 | 21.22 | 102.49 | 123.07 | 91.36 | 68.87, 68.91 | | 77.05 | 61.60 |
| **6a** ($D_2O$) | 137.80 | 101.08 | 22.07 | 105.20 | 125.37 | 95.03 | 71.11 | 70.21 | 85.36 | 61.63 |
| **13** ($D_2O$) | 137.75 | 100.93 | 21.91 | 105.13 | 125.20 | 94.82, dd ($J_{CC}$ = 5.7; $^1J_{CC}$ = 42) | 69.64–71.33, m ($^1J_{CC}$ = 39) | | 83.48, dm ($^1J_{CC}$ = 39) | 61.45, d ($^1J_{CC}$ = 41) |
| **5a** ($D_2O$) | 140.35 | 133.94 | 145.62 | 128.38 | 142.60 | 99.93 | 77.44 | 69.78 | 85.70 | 60.19 |
| **11** ($D_2O$) | 140.36 | 133.96 | 145.63 | 128.37 | 142.61 | 99.91, dd (J = 3.2; $^1J_{CC}$ = 40) | 77.42, t ($^1J_{CC}$ = 38) | 69.75, dt (J = 3.4; $^1J_{CC}$ = 40) | 87.67, t ($^1J_{CC}$ = 40) | 60.19, d ($^1J_{CC}$ = 40) |
| **3b** ($D_2O$) | 140.89 | 137.62 | 147.52 | 128.16 | 141.73 | 96.98 | 76.39 | 69.72 | 82.61 | 62.74 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **4b** (acetone-$d_6$) | 138.32 | 100.34 | 22.24 | 104.63 | 125.74 | 92.93 | 70.77 | 70.56 | 78.98 | 63.41 |
| **5b** ($D_2O$) | 140.87 | 137.26 | 146.85 | 127.91 | 141.31 | 99.56 | 77.42 | 69.97 | 87.58 | 60.39 |
| **6b** ($D_2O$) | 136.42 | 105.92 | 23.17 | 104.69 | 126.11 | 95.15 | 70.91 | 70.31 | 83.22 | 61.69 |
| **9** ($CDCl_3$) | | | | | | 93.43–94.61 (α), m ($^1J_{CC}$ = 45) | 68.36–70.00 (α), m | | 81.14–81.99 (α), m ($^1J_{CC}$ = 42) | 63.25 (α), 63.91 (β), both d ($^1J_{CC}$ = 43) |
| | | | | | | 98.15 (β), dd ($J_{CC}$ = 3.1; $^1J_{CC}$ = 47) | 74.09 (β), dd ($^1J_{CC}$ = 38; 47) | 70.47 (β), t ($^1J_{CC}$ = 40) | 79.25 (β), dd ($^1J_{CC}$ = 40; 43) | |

# NMR, MS and HRMS SPECTRA of SYNTHESIZED COMPOUNDS

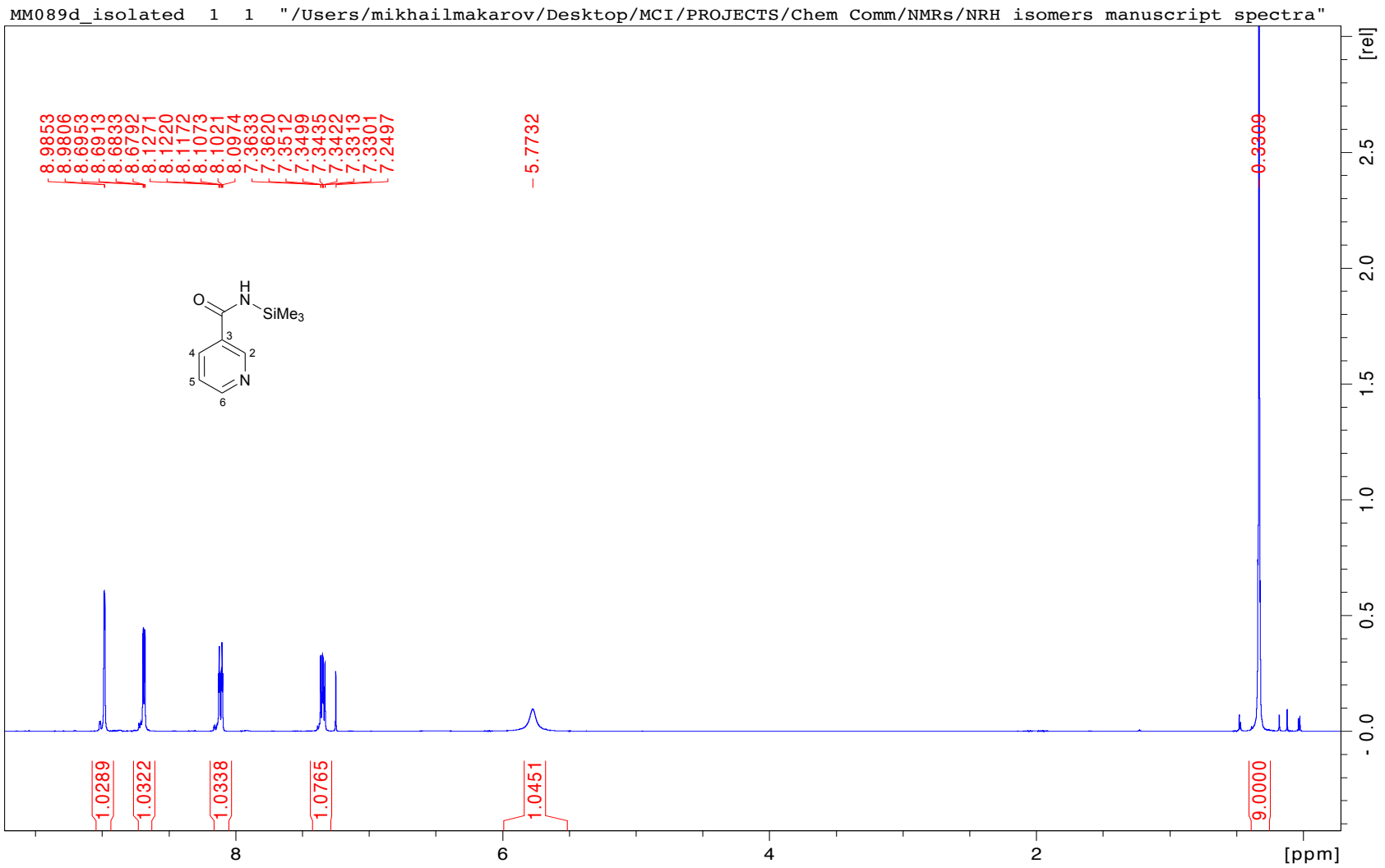



**Figure 1.** $^{1}$H NMR ($CDCl_3$) of *N*-(trimethylsilyl)nicotinamide (**2a**).

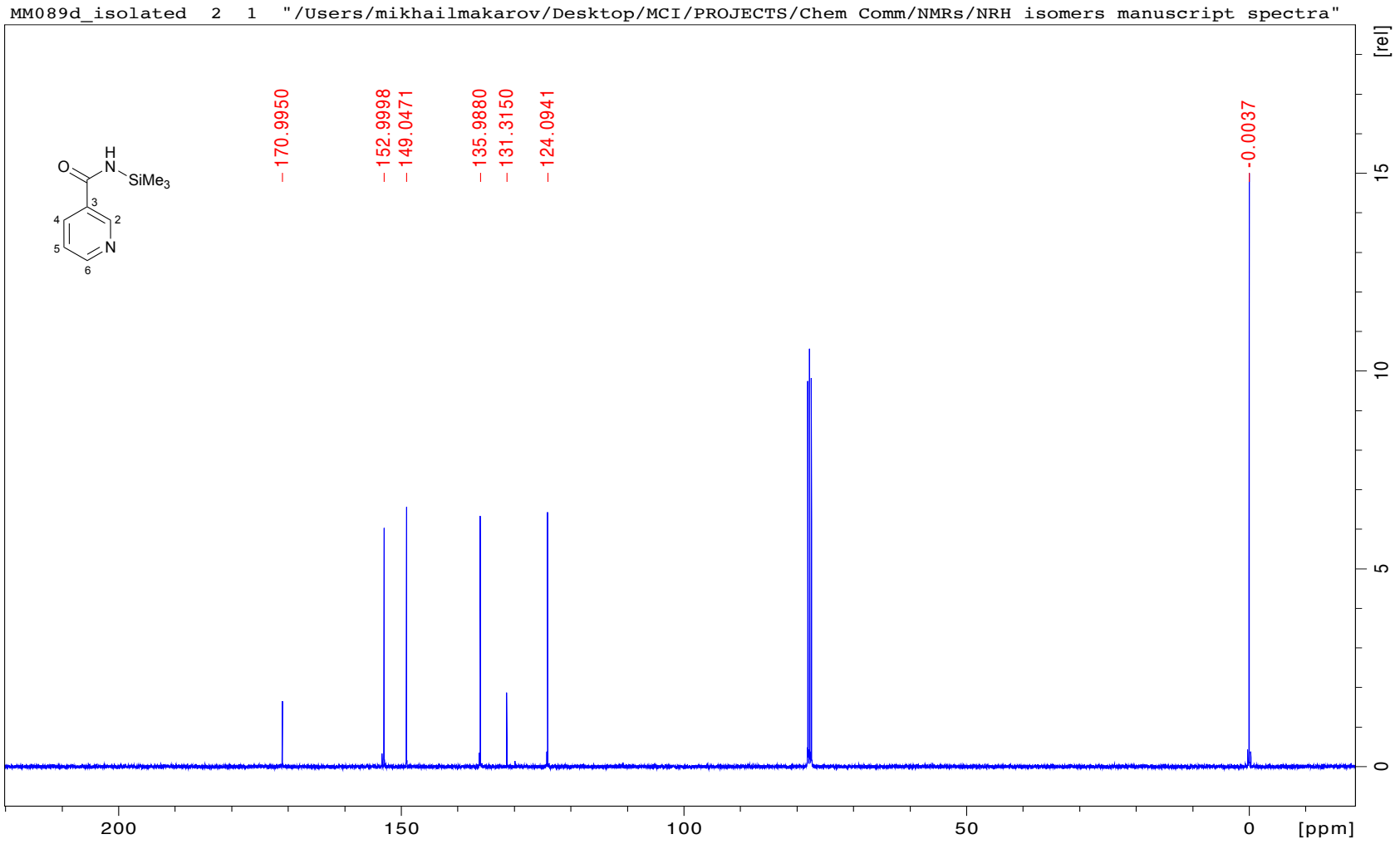



**Figure 2.** $^{13}C$ NMR ($CDCl_3$) of *N*-(trimethylsilyl)nicotinamide (**2a**).

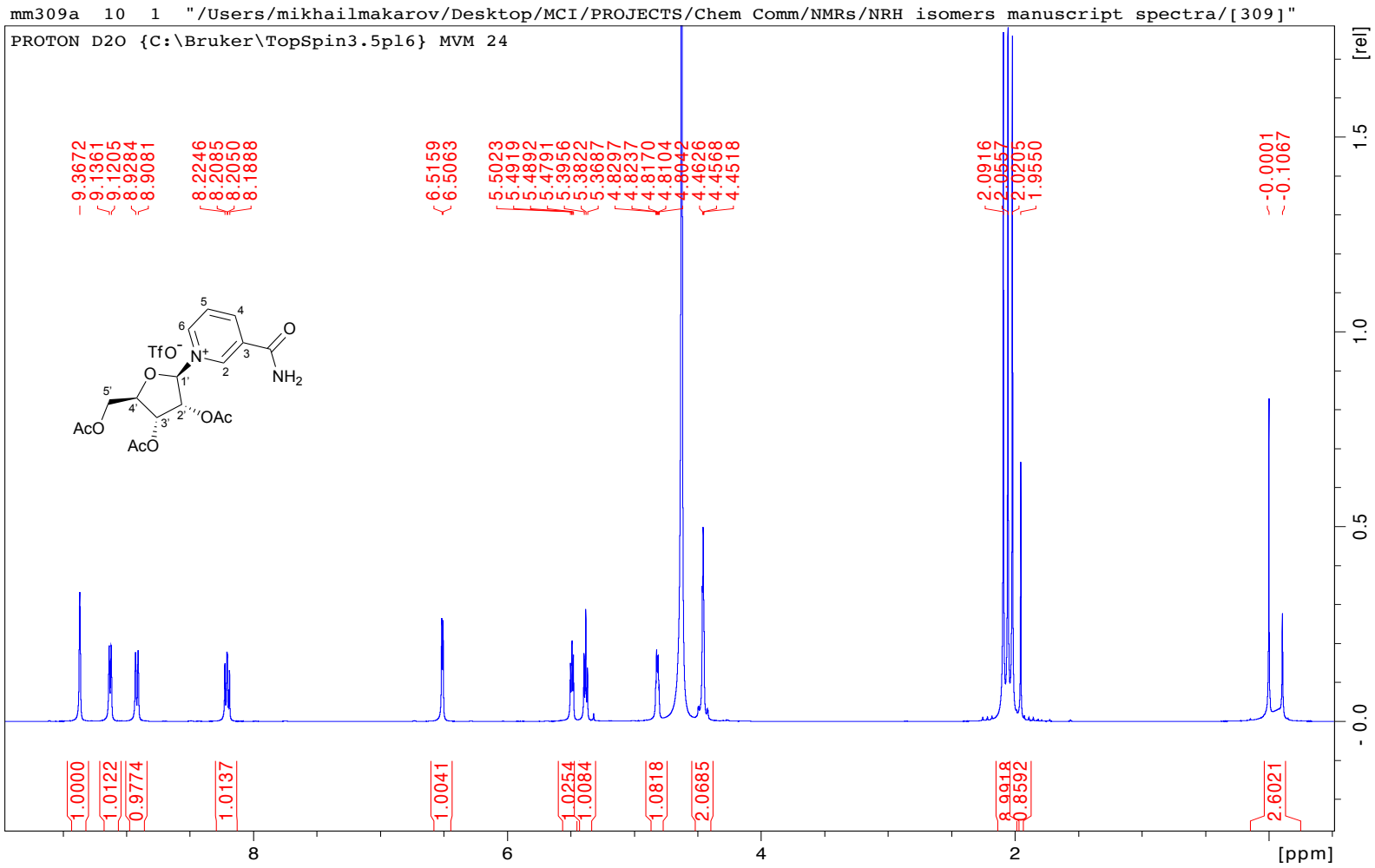



**Figure 3.** $^{1}H$ NMR ($D_2O$) of NR triacetate triflate (**3a**), general view.

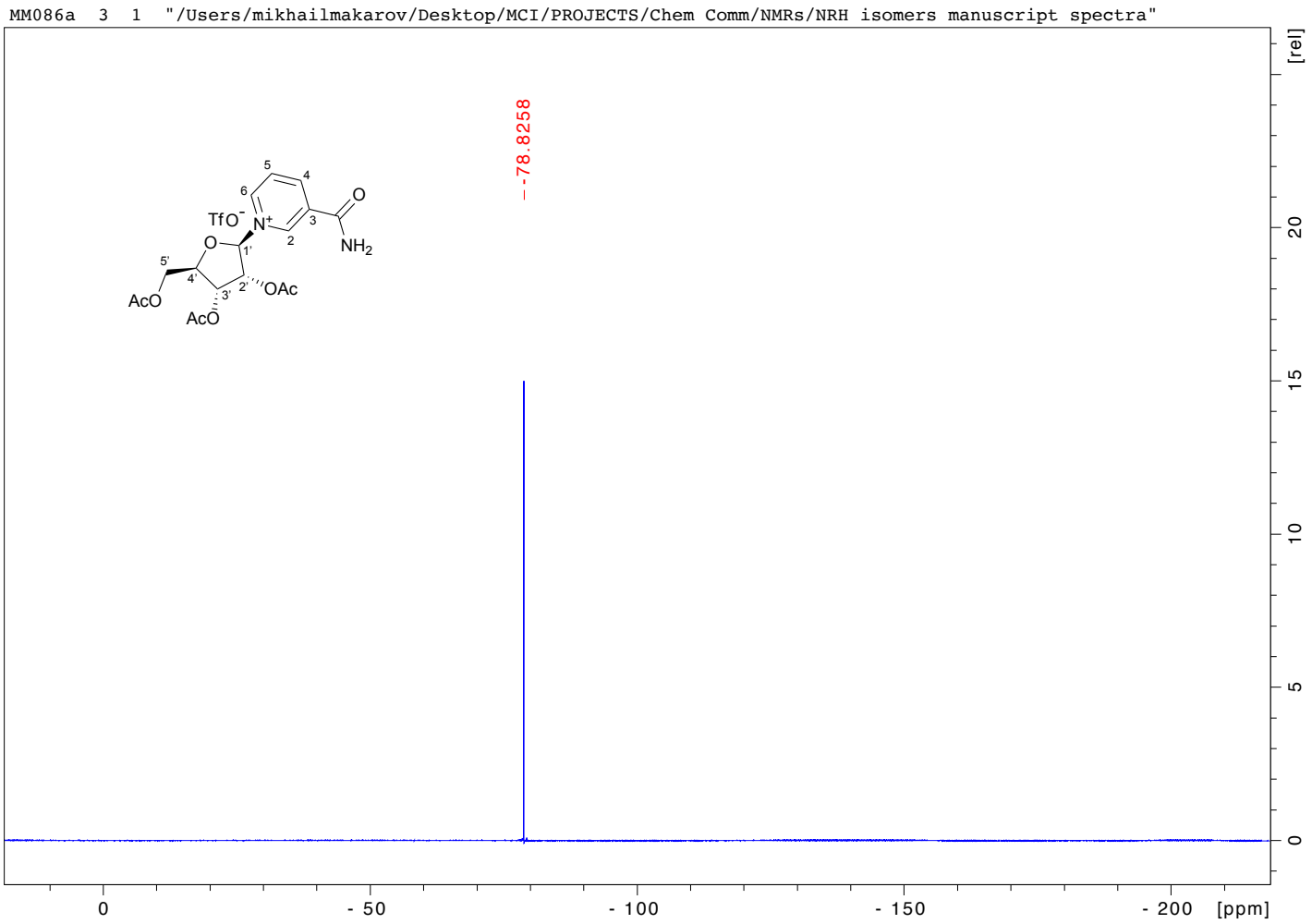



**Figure 4.** $^{19}F$ NMR ($D_2O$) of NR triacetate triflate (**3a**), general view.

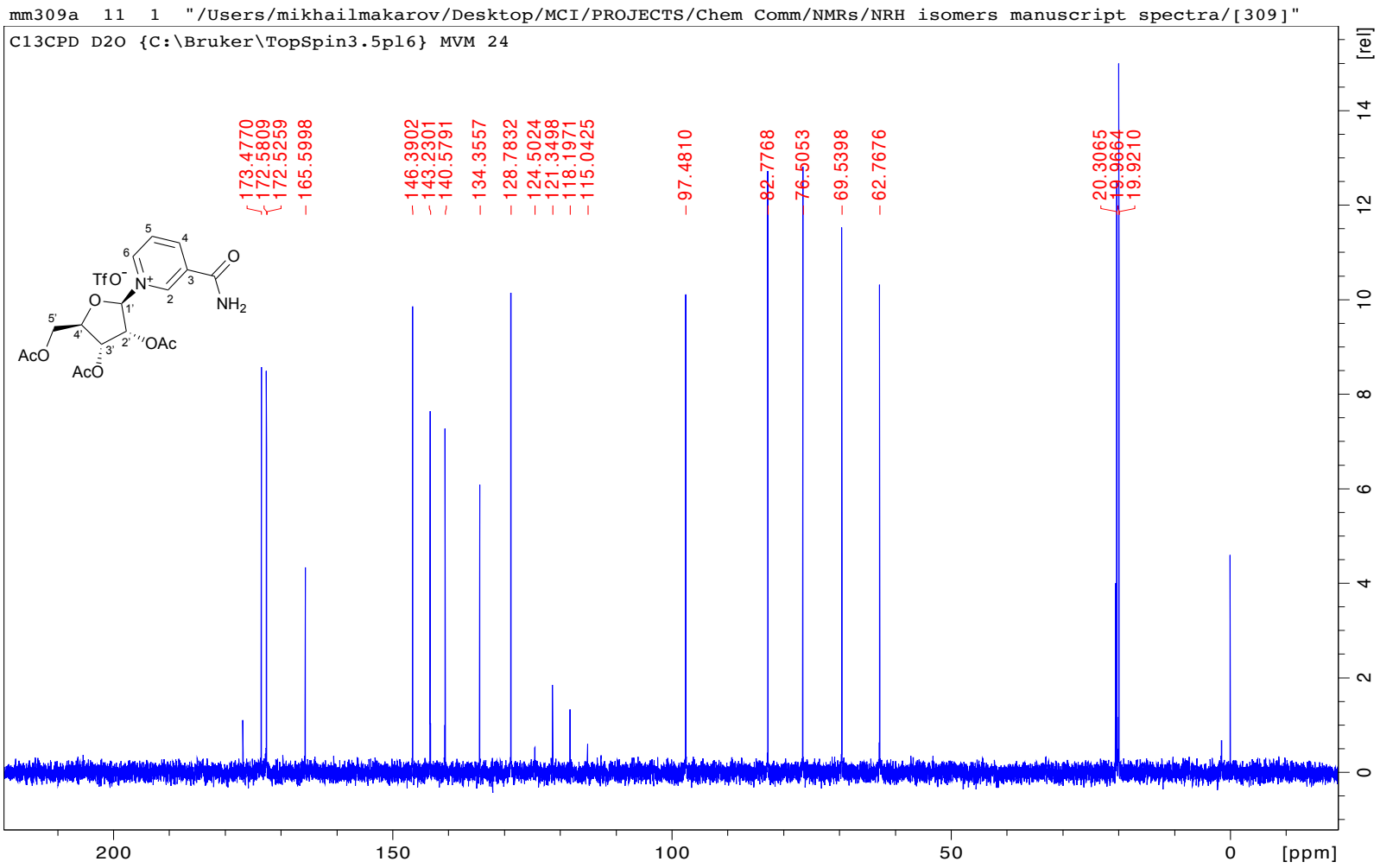



**Figure 5.** $^{13}C$ NMR ($D_2O$) of NR triacetate triflate (**3a**), general view.

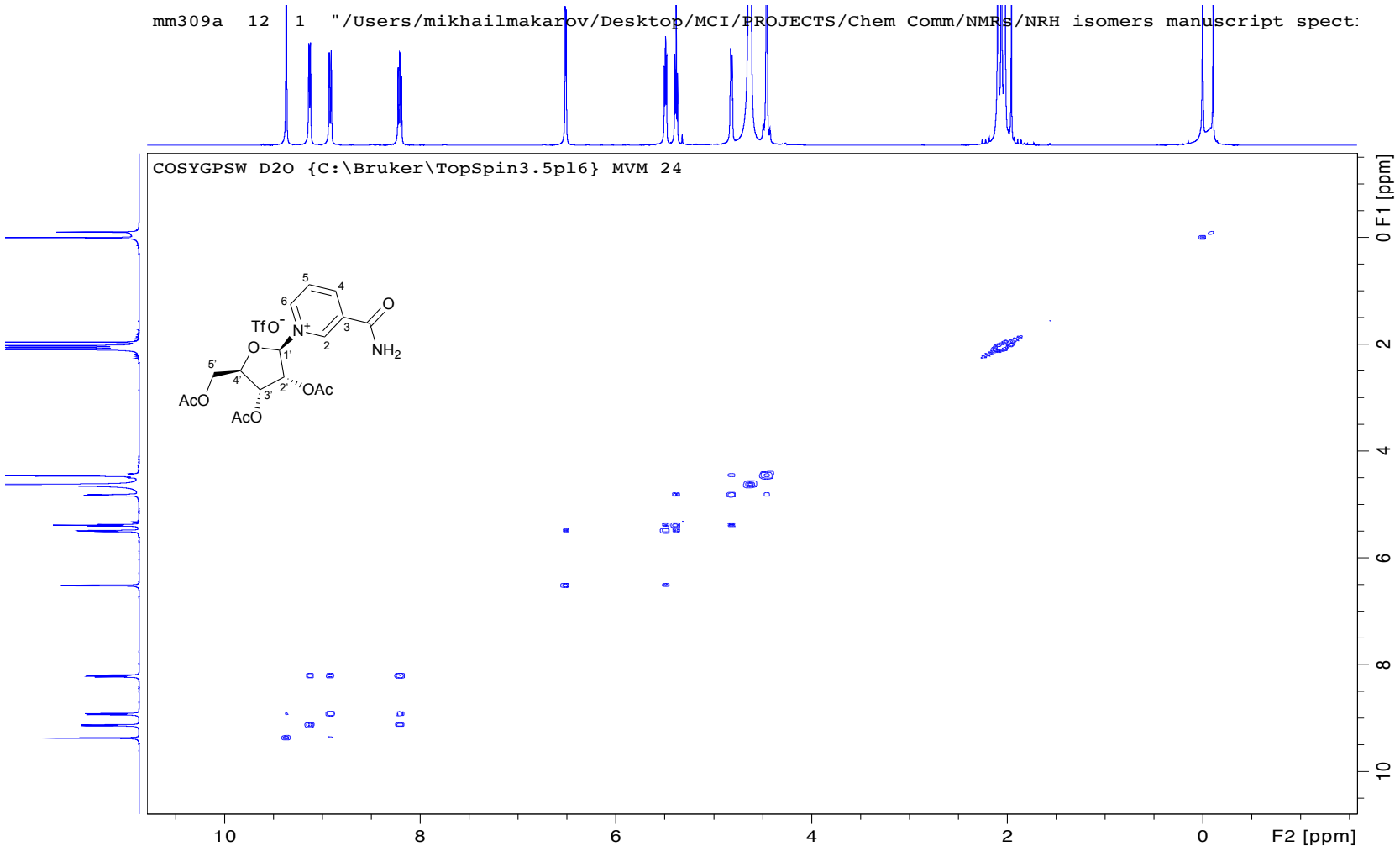



**Figure 6.** COSY ($D_2O$) of NR triacetate triflate (**3a**).

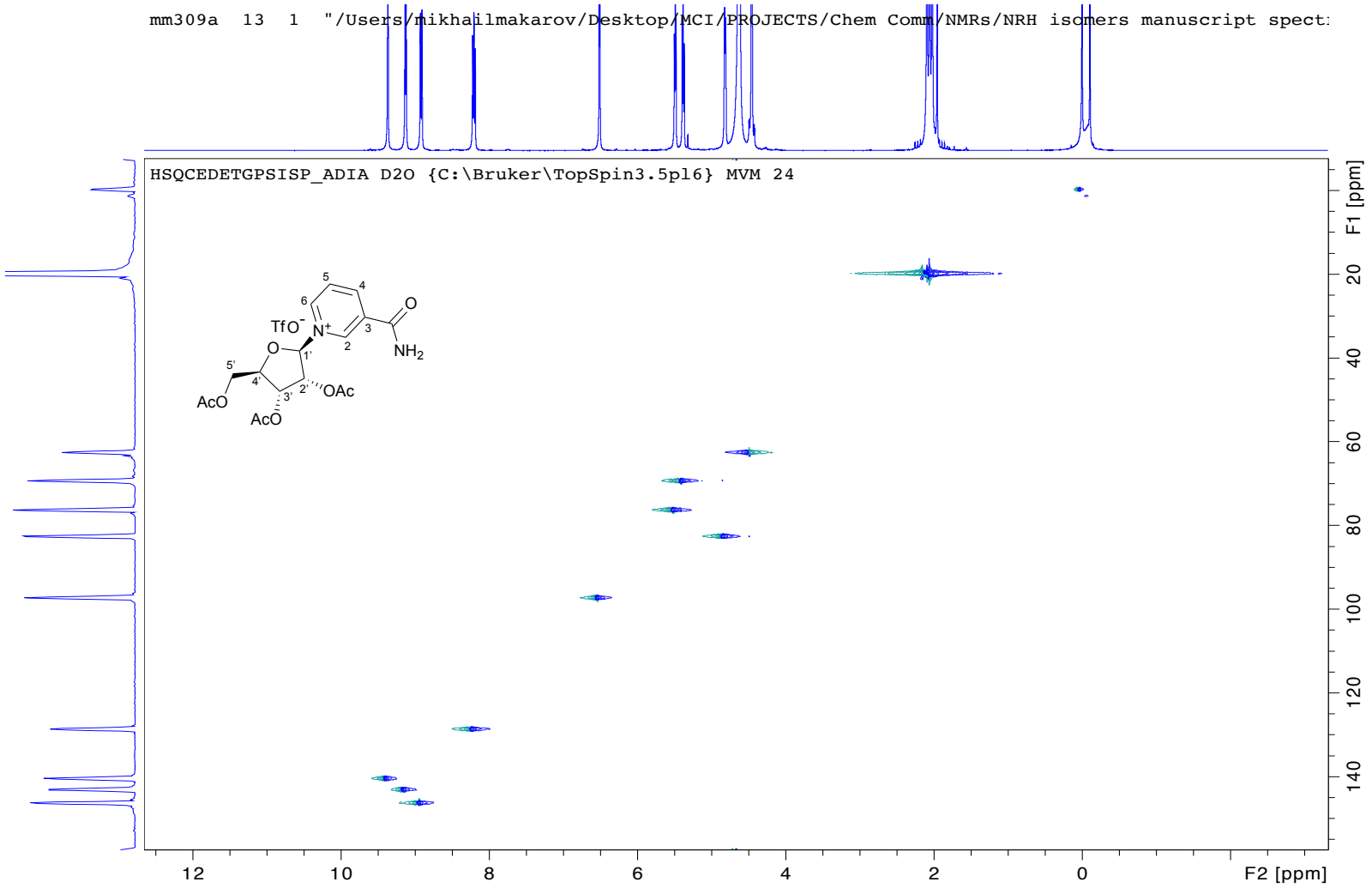



**Figure 7.** HSQC ($D_2O$) of NR triacetate triflate (**3a**).

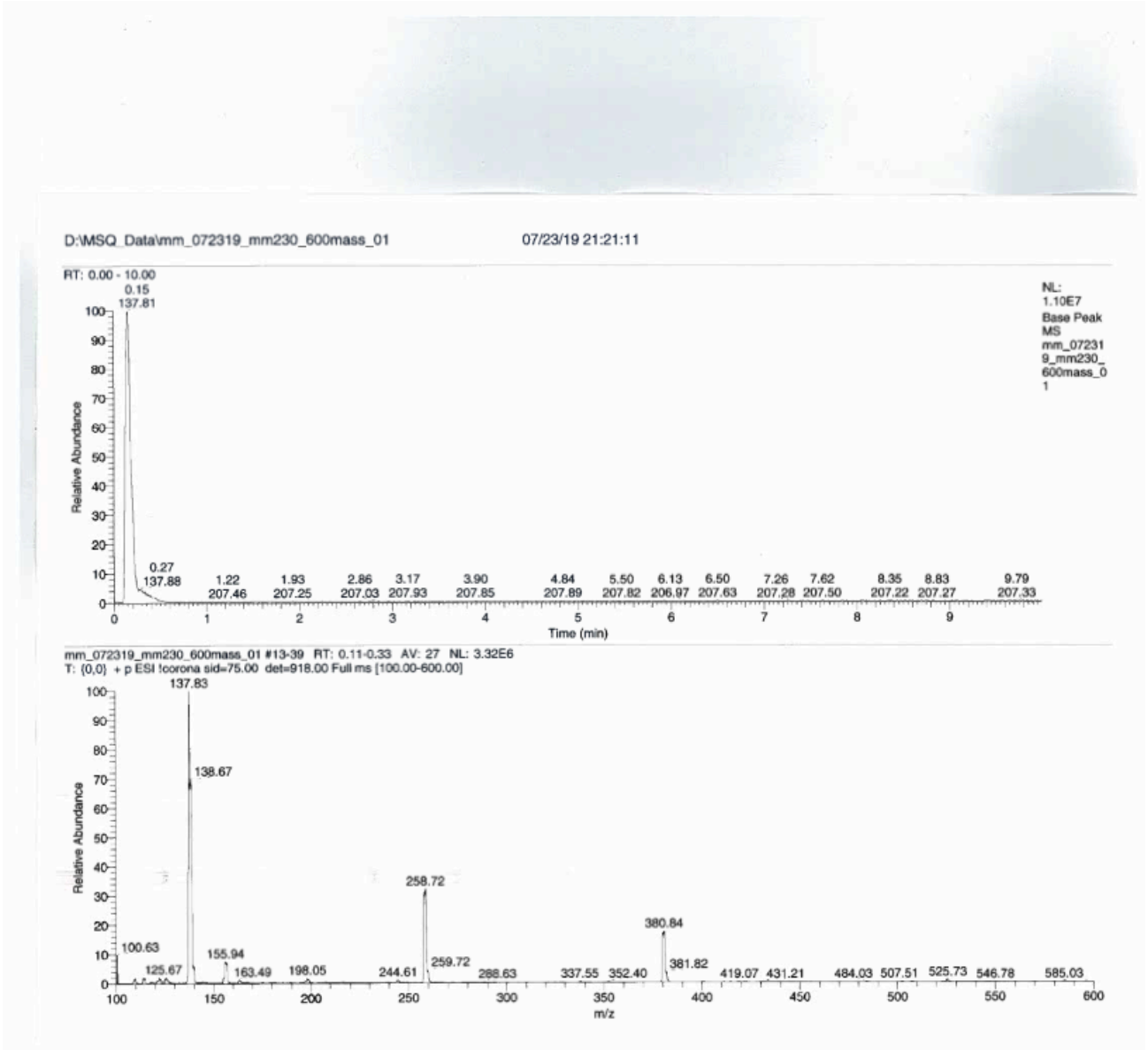



**Figure 8.** MS of NR triacetate triflate (**3a**) in 1:1 $H_2O$/ACN.

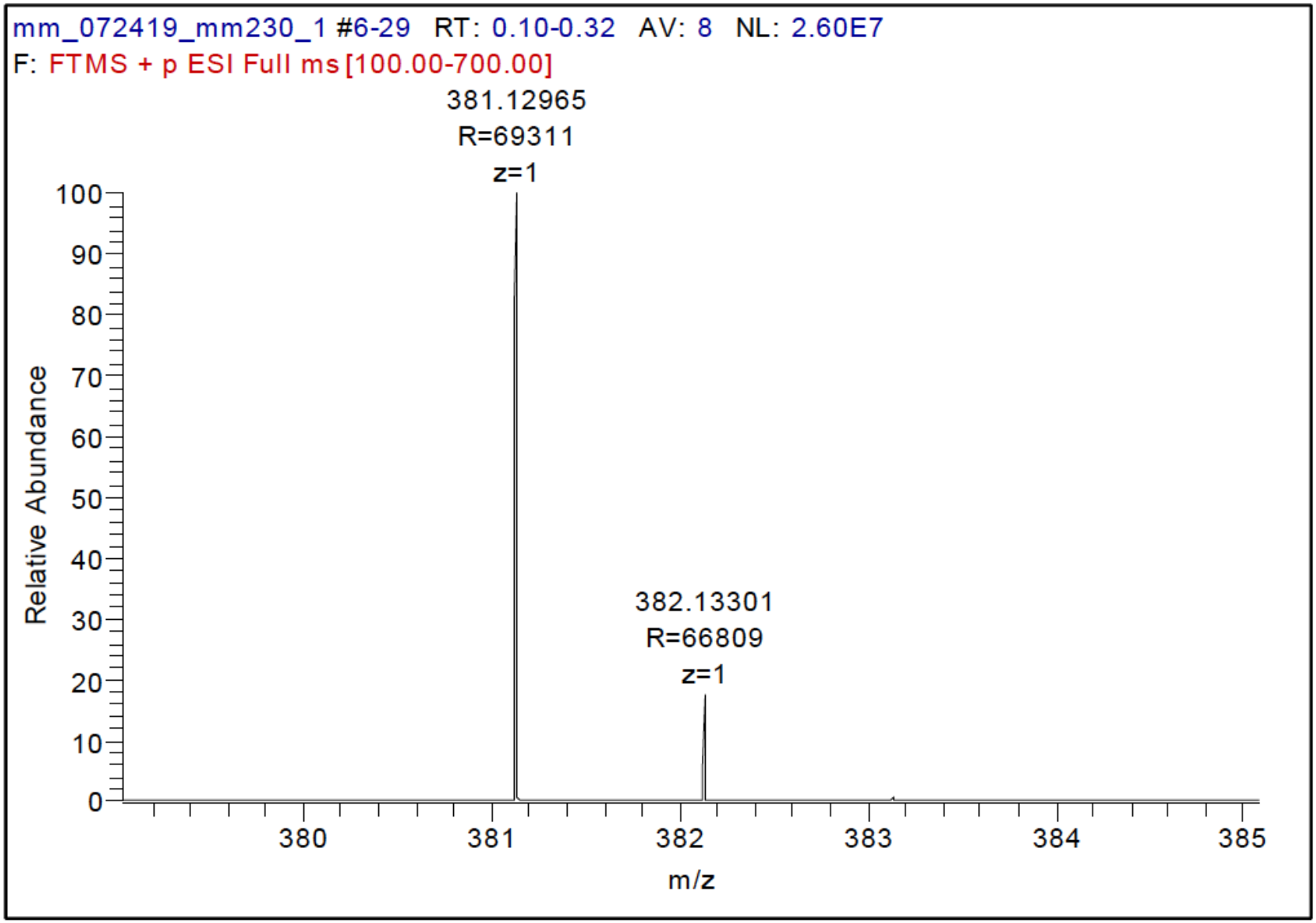



**Figure 9.** HRMS of NR triacetate triflate (**3a**) in 1:1 $H_2O$/ACN.

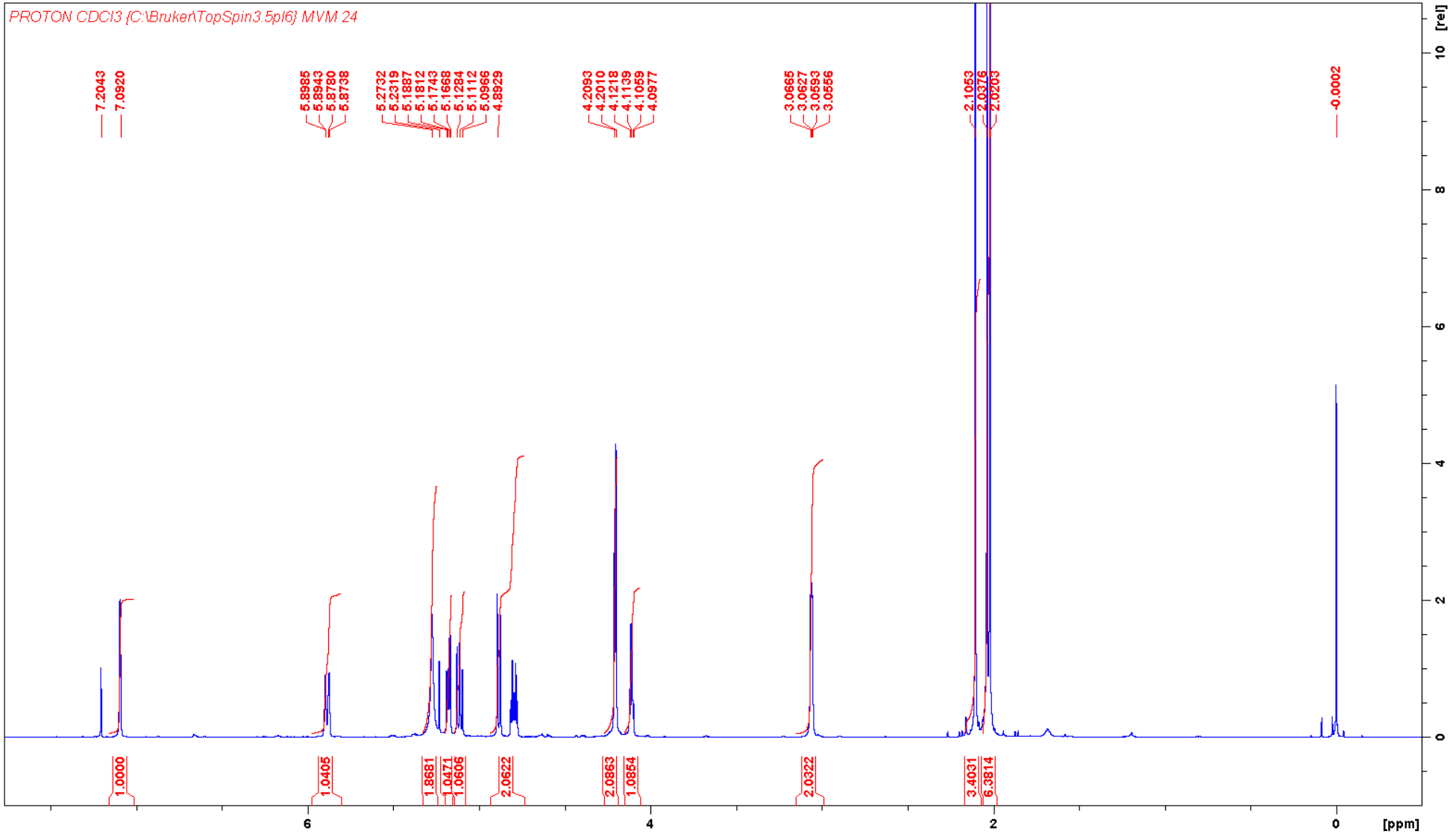



**Figure 10.** $^{1}$H NMR ($CDCl_3$) of NRH triacetate (**4a**), general view

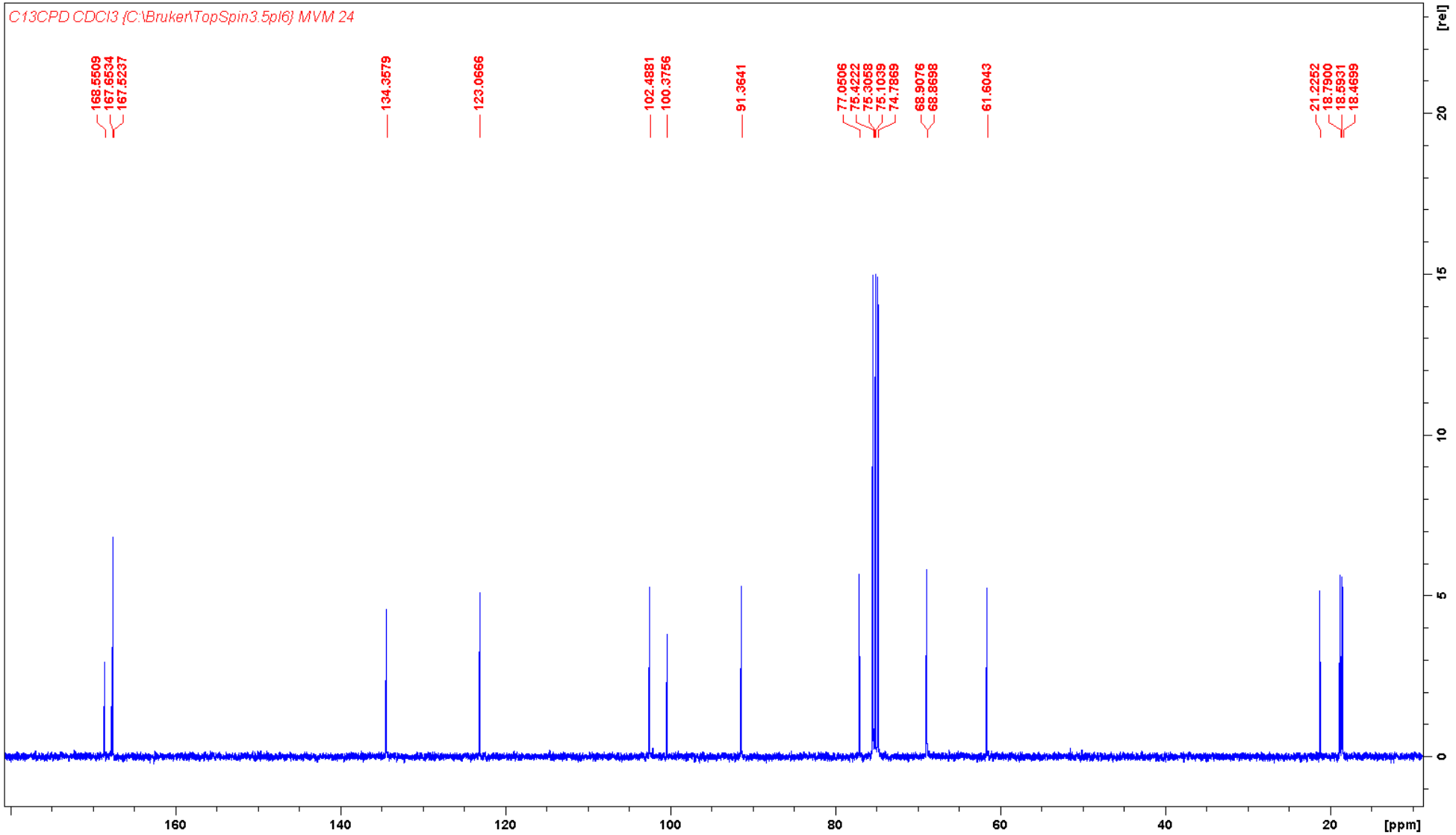



**Figure 11**. $^{13}C$ NMR ($CDCl_3$) of NRH triacetate (**4a**), general view

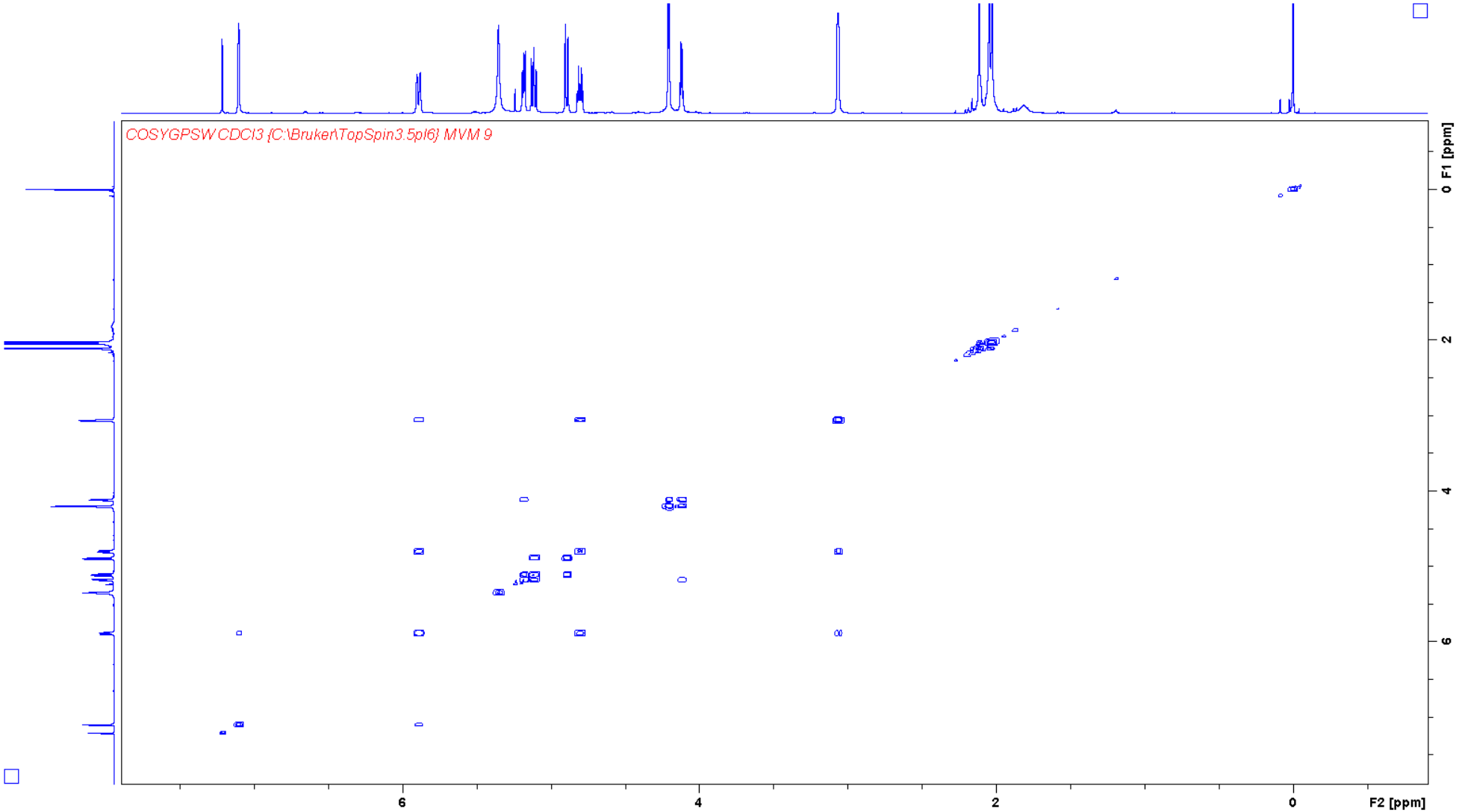



**Figure 12.** COSY ($CDCl_3$) of NRH triacetate (**4a**).

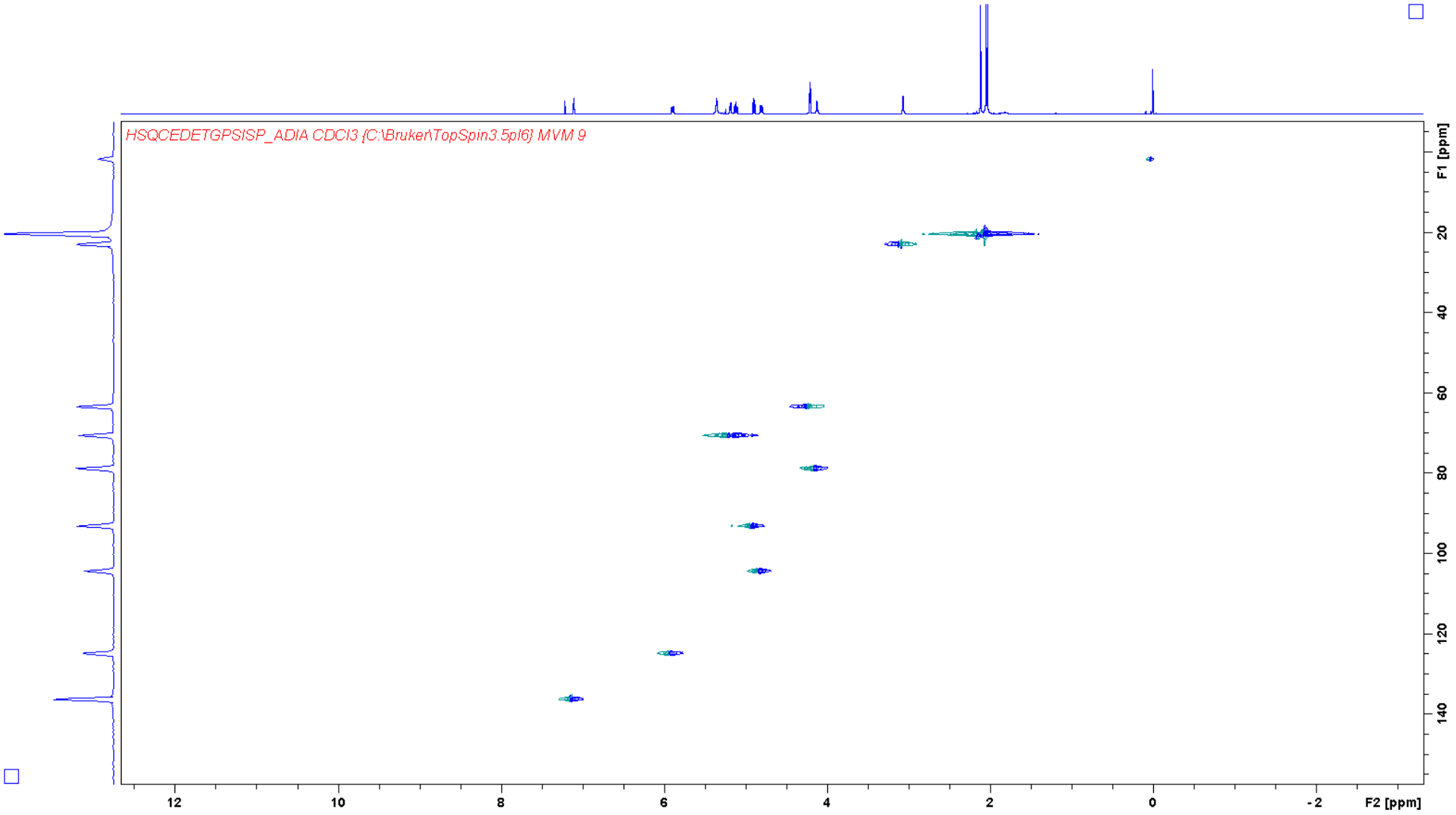



**Figure 13.** HSQC ($CDCl_3$) of NRH triacetate (**4a**).

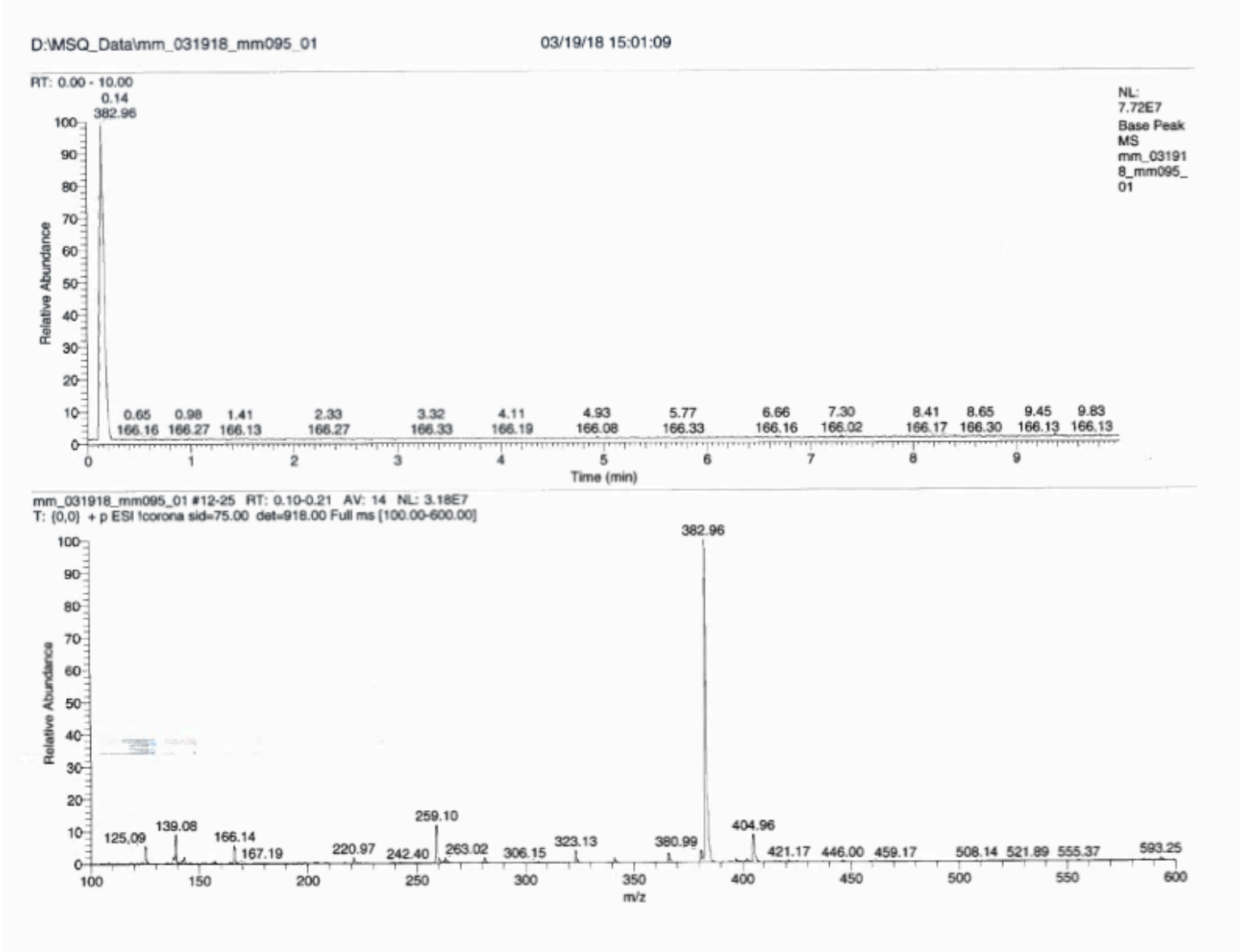



**Figure 14.** MS spectrum of NRH triacetate (**4a**).

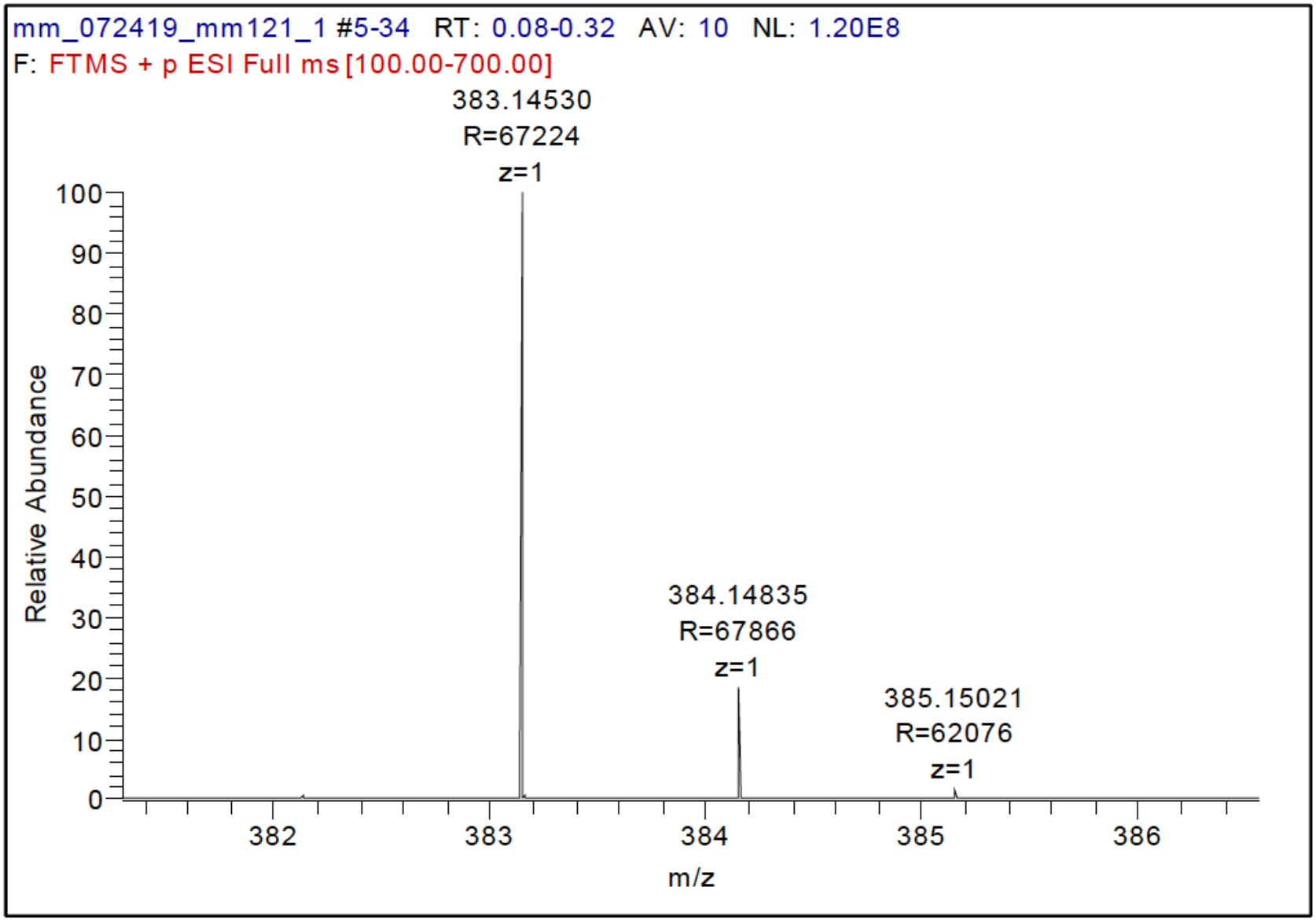



**Figure 15.** HRMS spectrum of NRH triacetate (**4a**) in 1:1 $H_2O$/ACN.

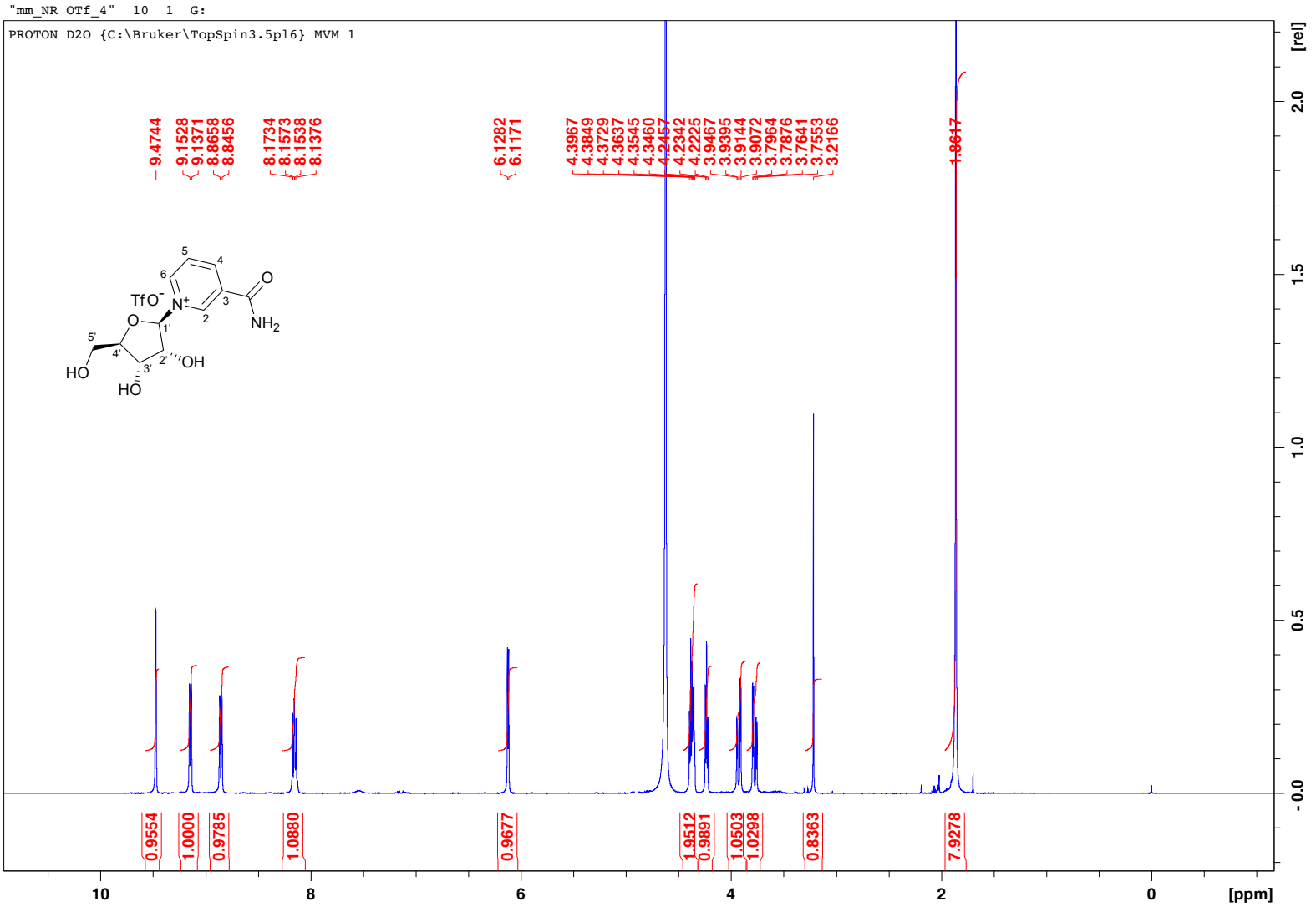



**Figure 16.** $^{1}H$ NMR ($D_2O$) of NR triflate (**5a**), general view

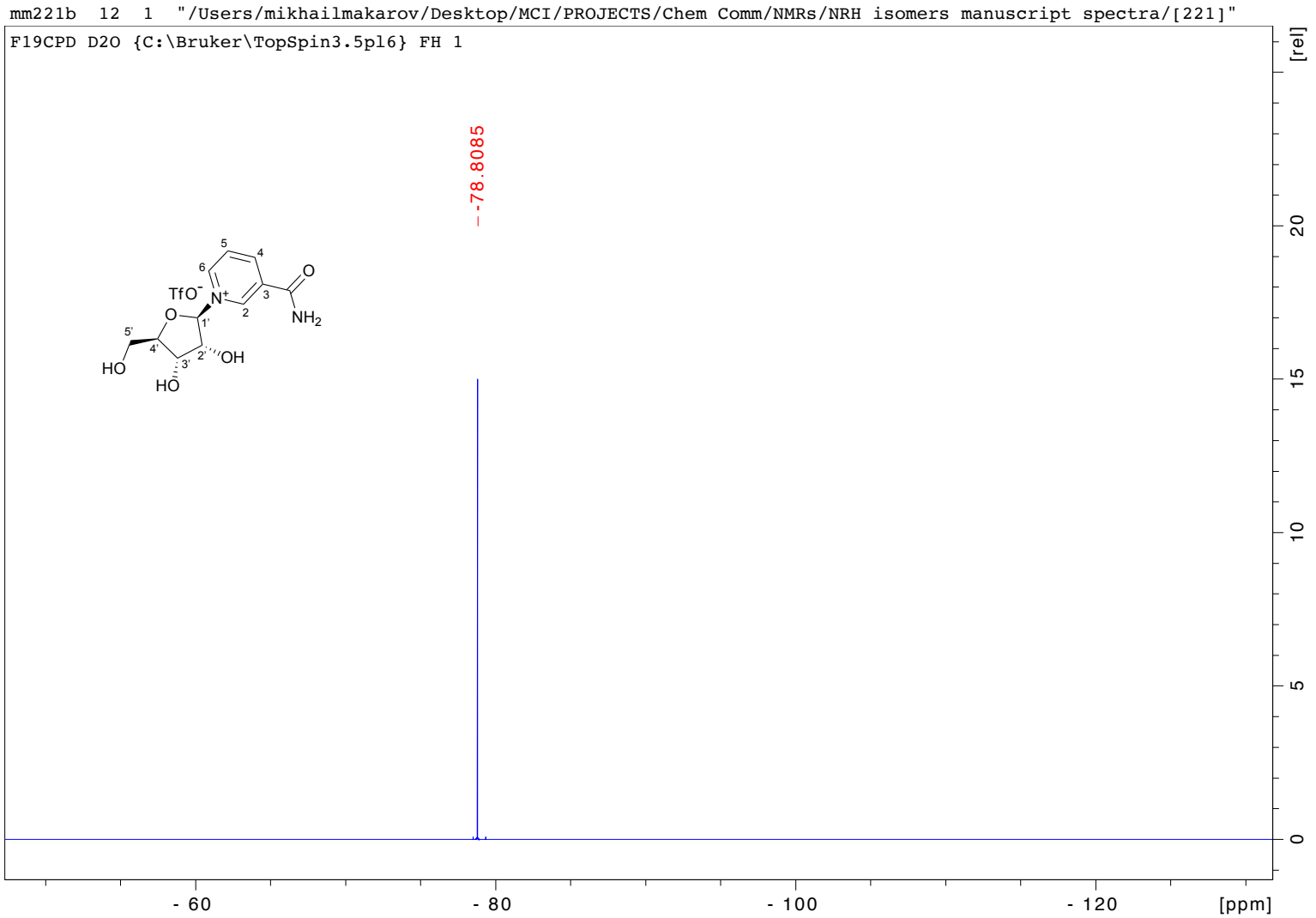



**Figure 17.** $^{19}F$ NMR ($D_2O$) of NR triflate (**5a**), general view

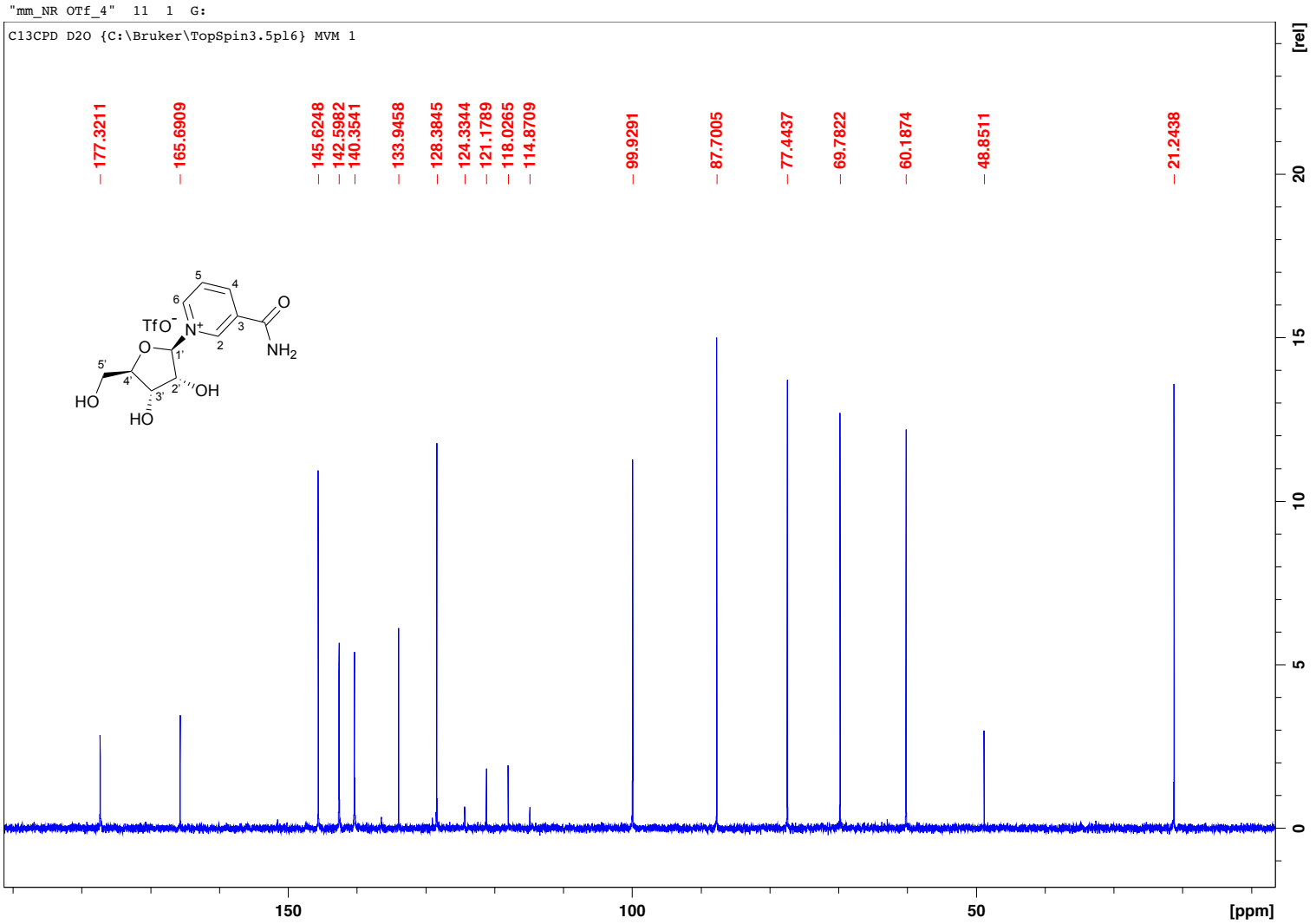



**Figure 18.** $^{13}C$ NMR ($D_2O$) of NR triflate (**5a**), general view

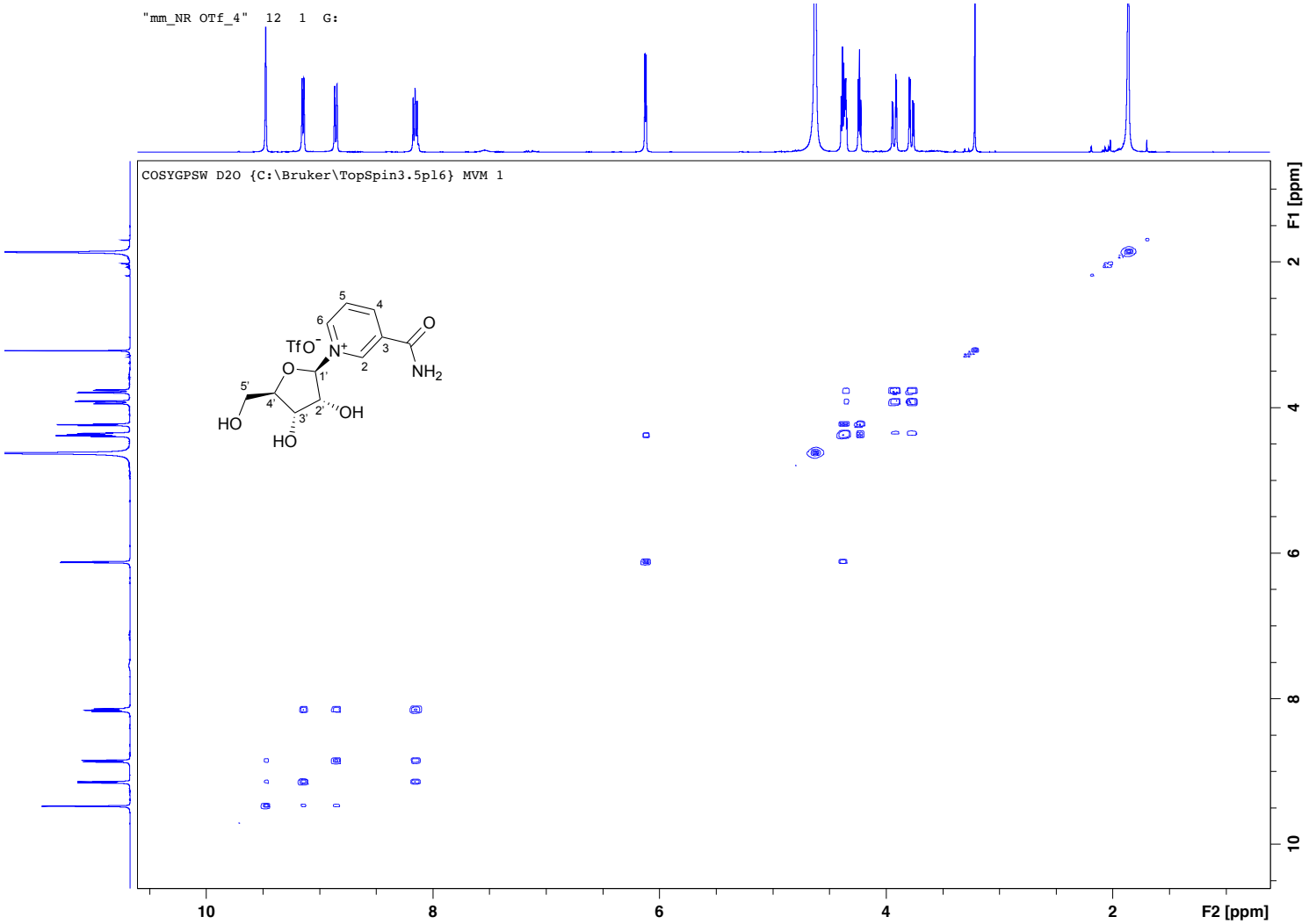



**Figure 19.** COSY ($D_2O$) of NR triflate (**5a**).

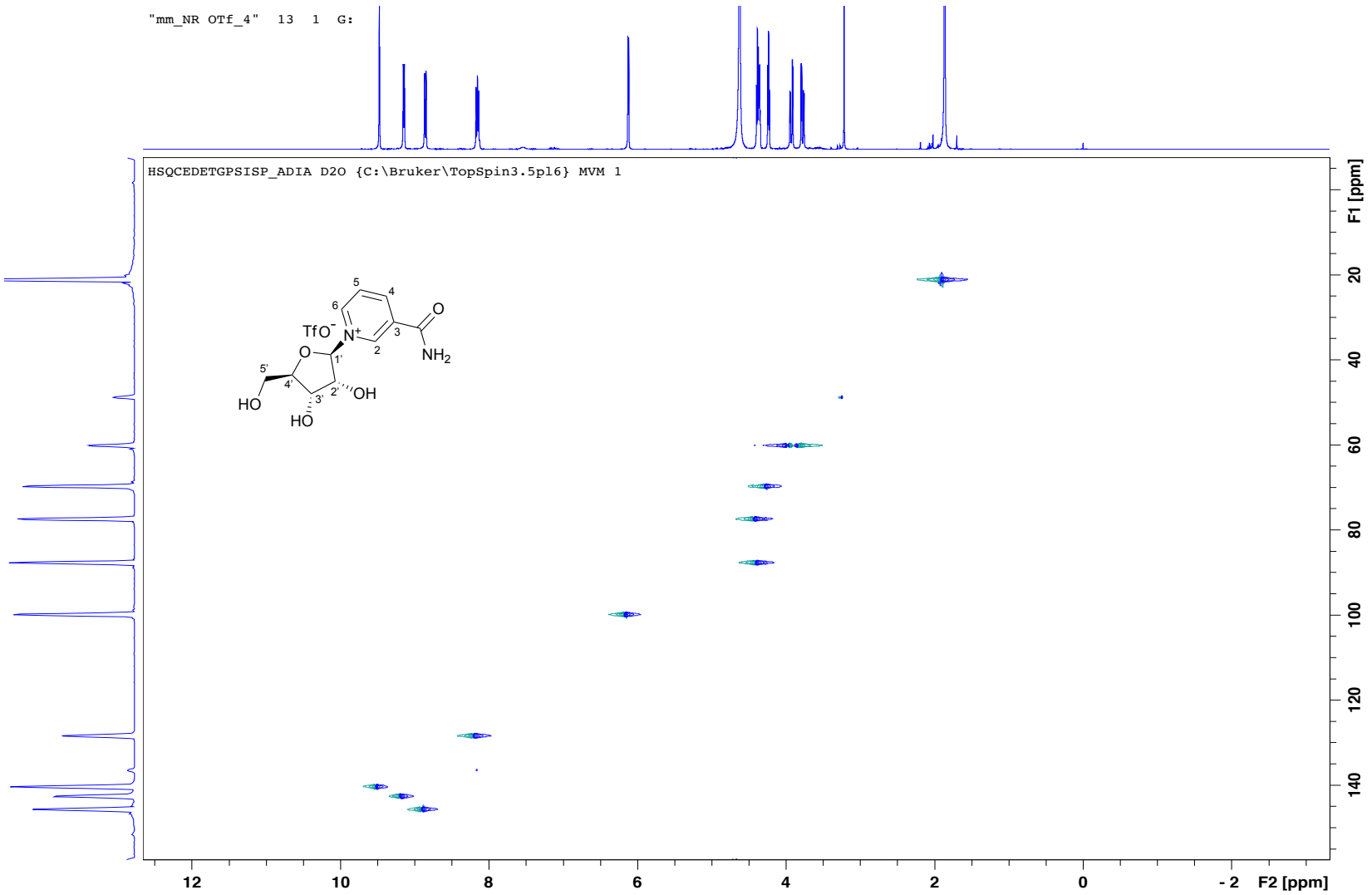



**Figure 20.** HSQC ($D_2O$) of NR triflate (**5a**).

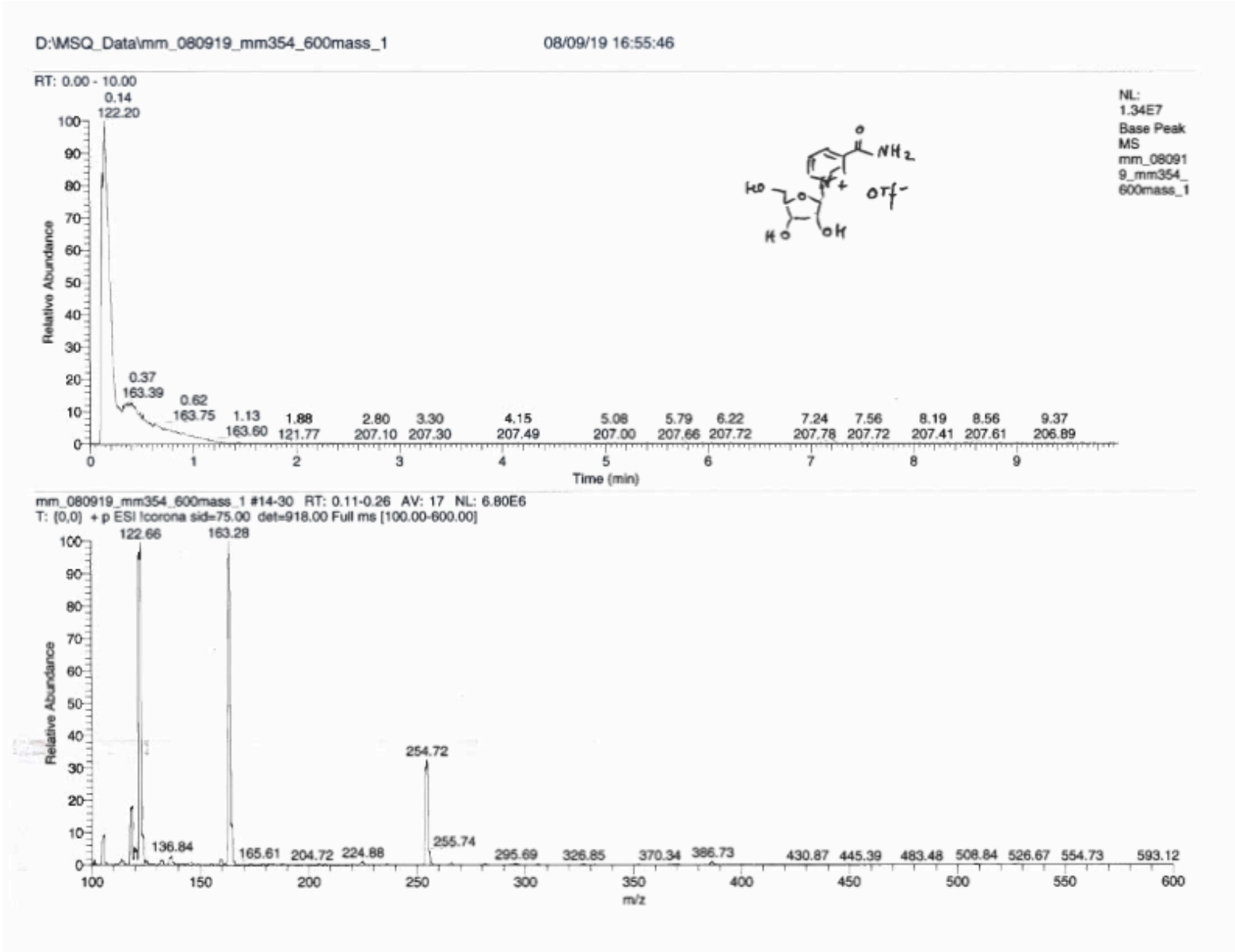



**Figure 21.** MS of NR triflate (**5a**) in 1:1 $H_2O$/ACN.

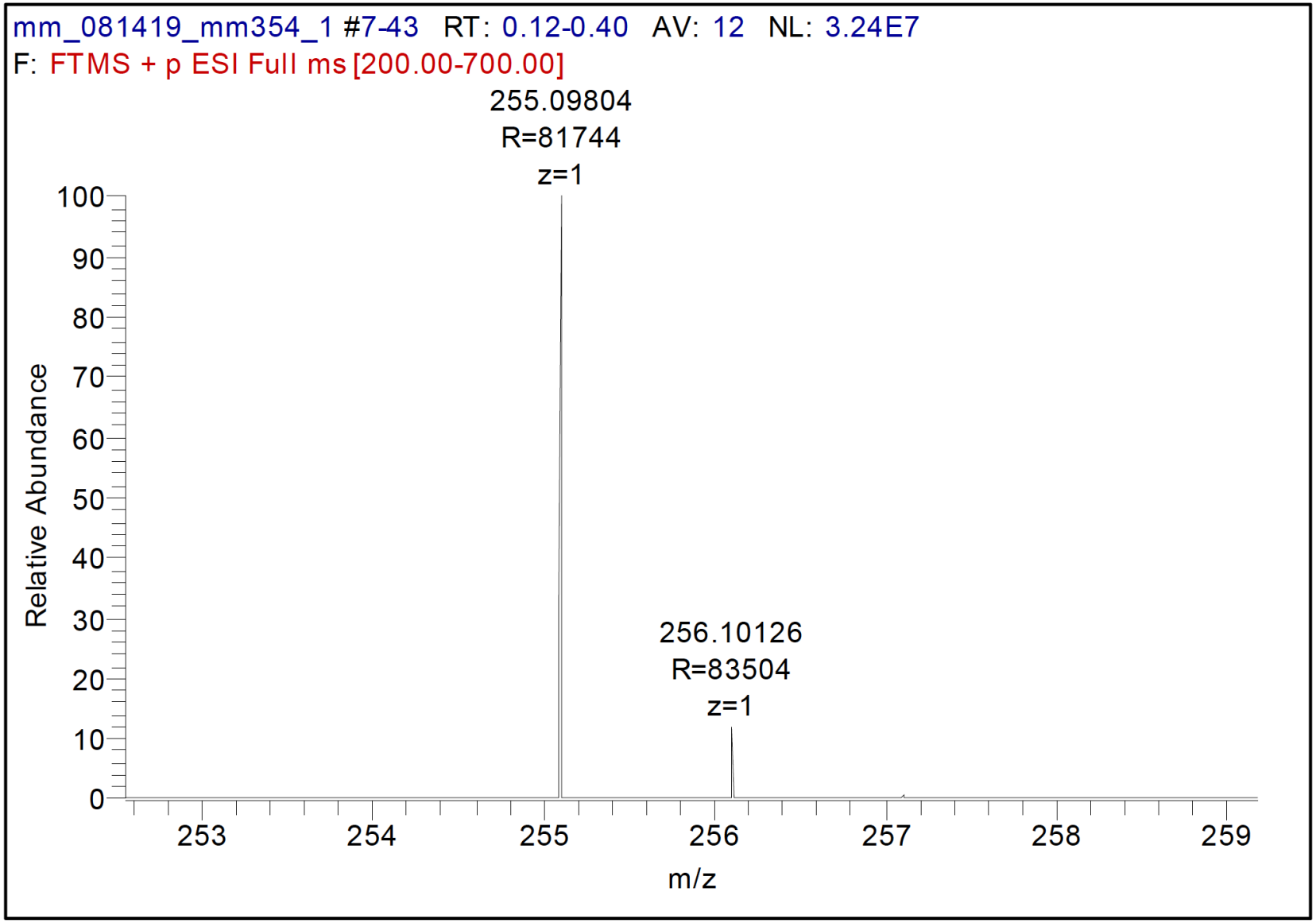



**Figure 22.** HRMS of NR triflate (**5a**) in 1:1 $H_2O$/ACN.

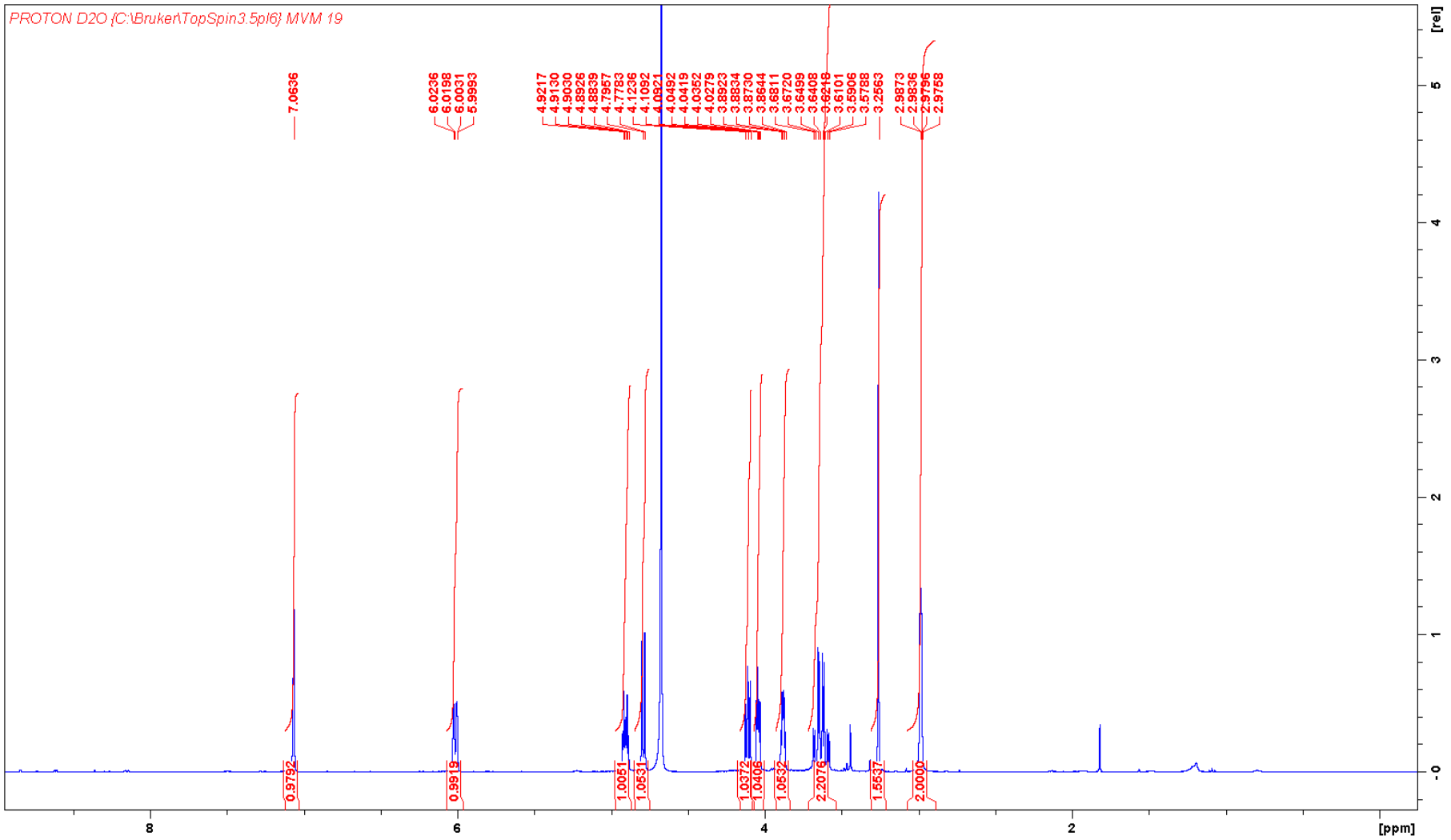



**Figure 23.** $^{1}H$ NMR ($D_2O$) of NRH (**6a**), general view.

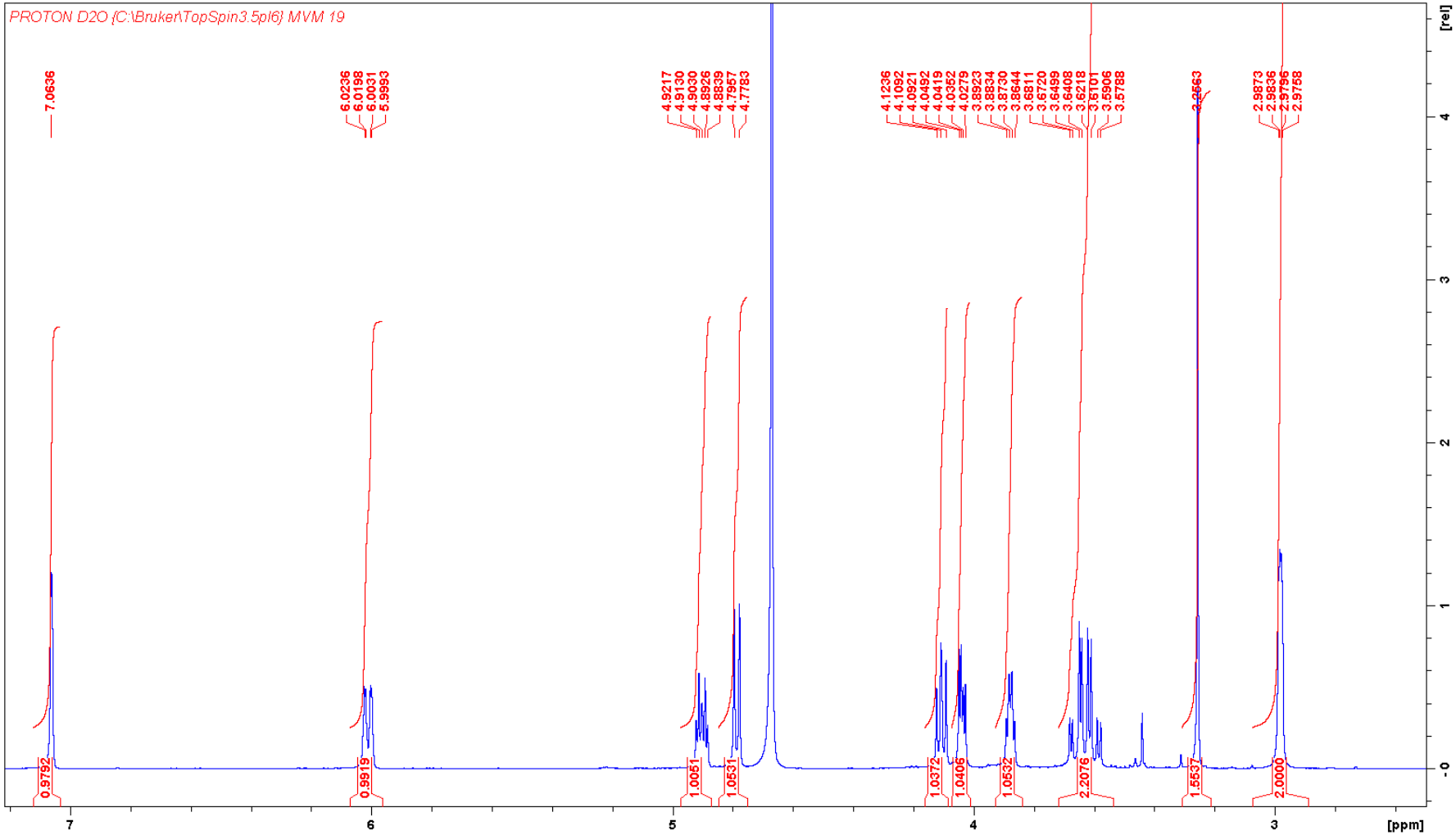



**Figure 24.** $^{1}H$ NMR ($D_2O$) of NRH (**6a**), view from ca. 2.5 to 7.1 ppm.

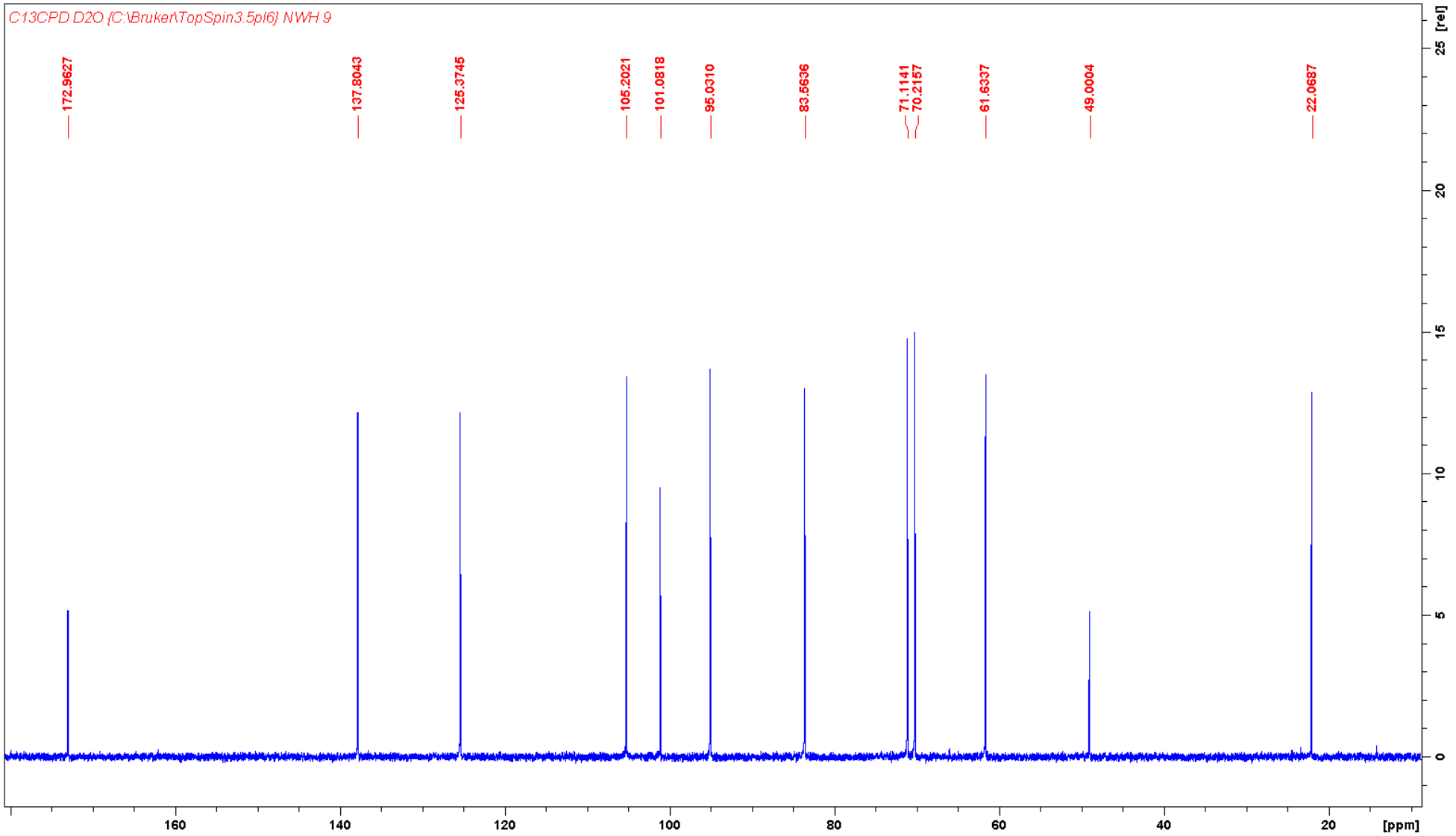



**Figure 25.** $^{13}C$ NMR ($D_2O$) of NRH (**6a**), general view.

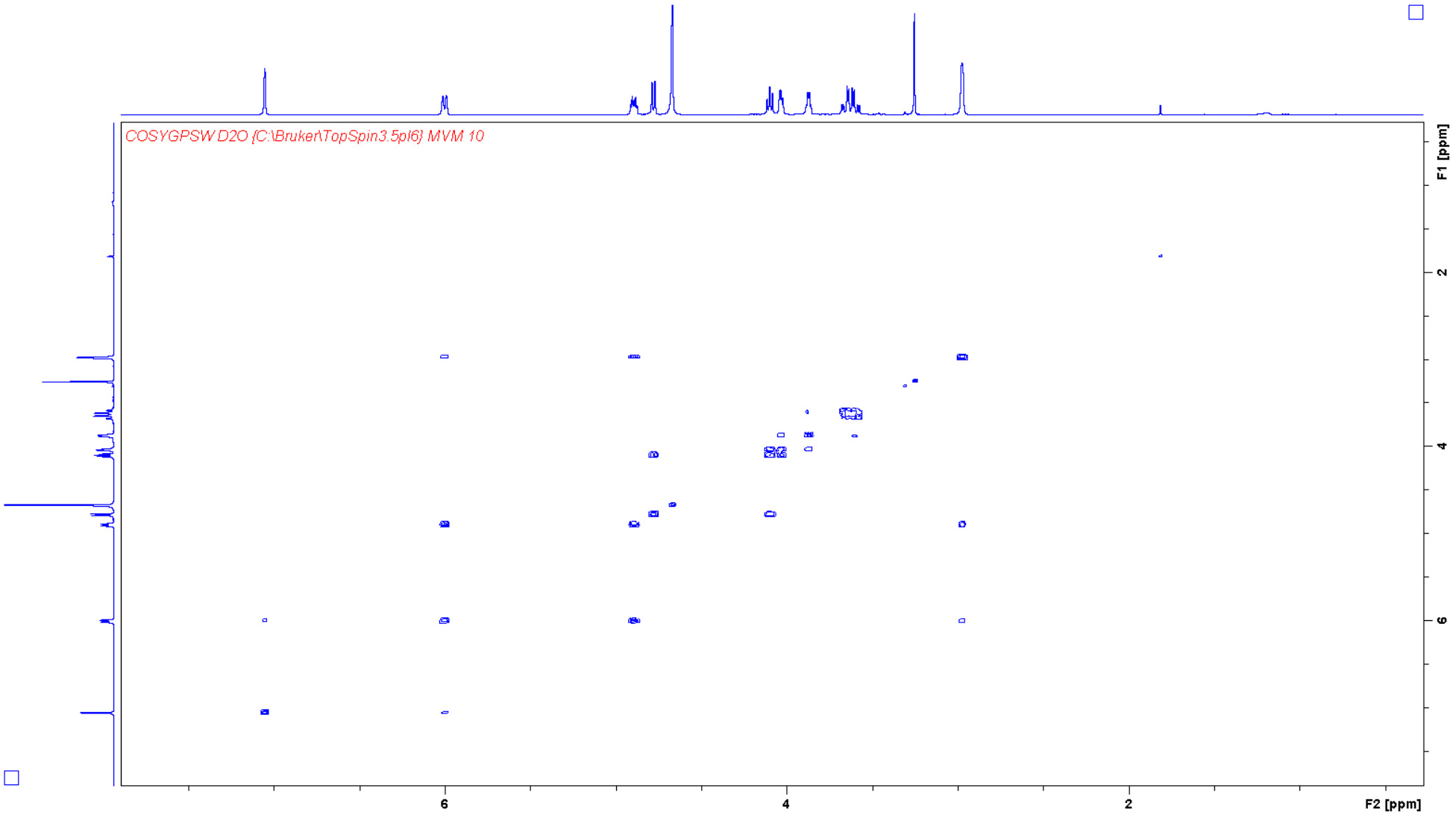



**Figure 26.** COSY ($D_2O$) of NRH (**6a**).

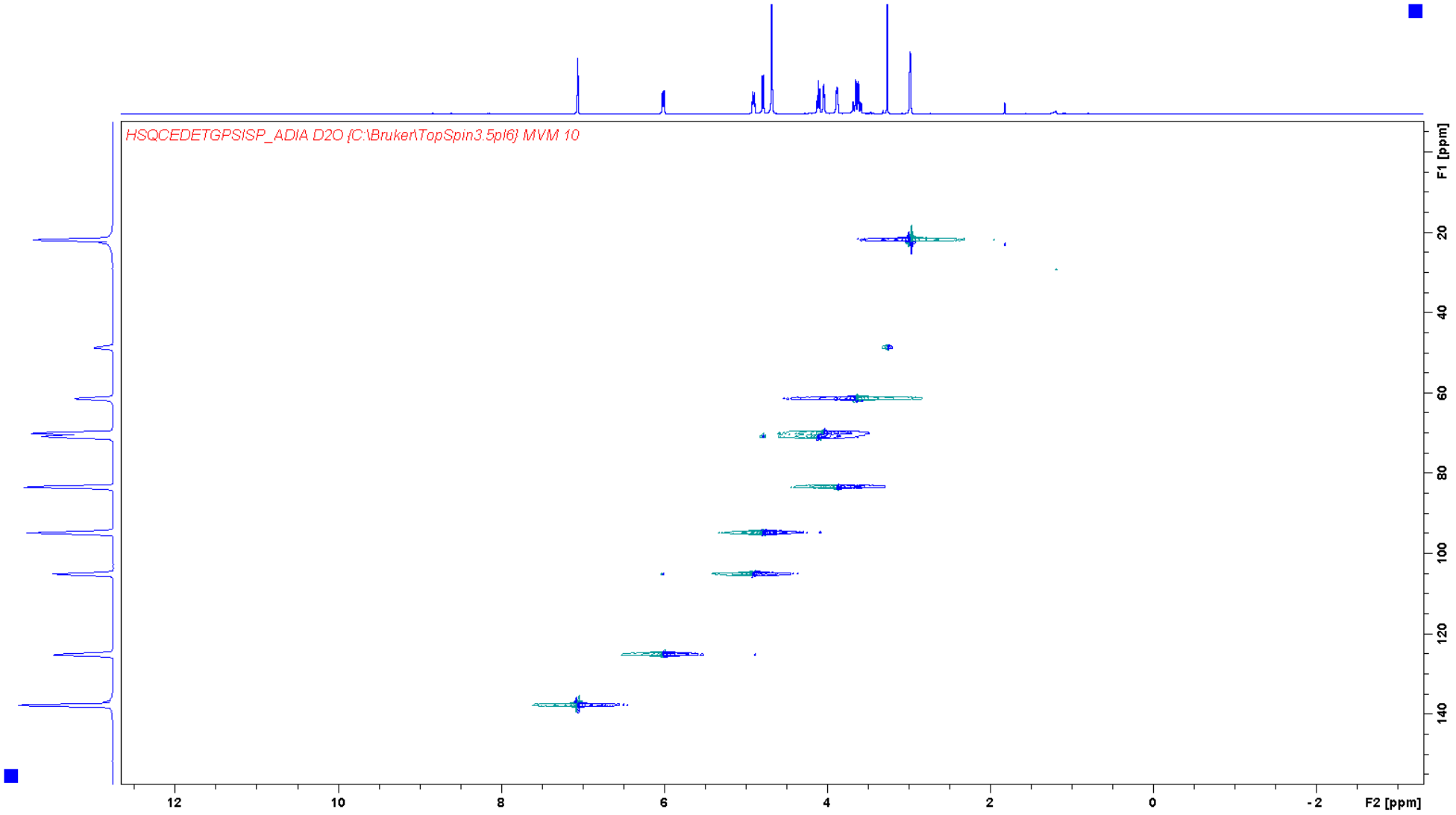



**Figure 27.** HSQC ($D_2O$) of NRH (**6a**).

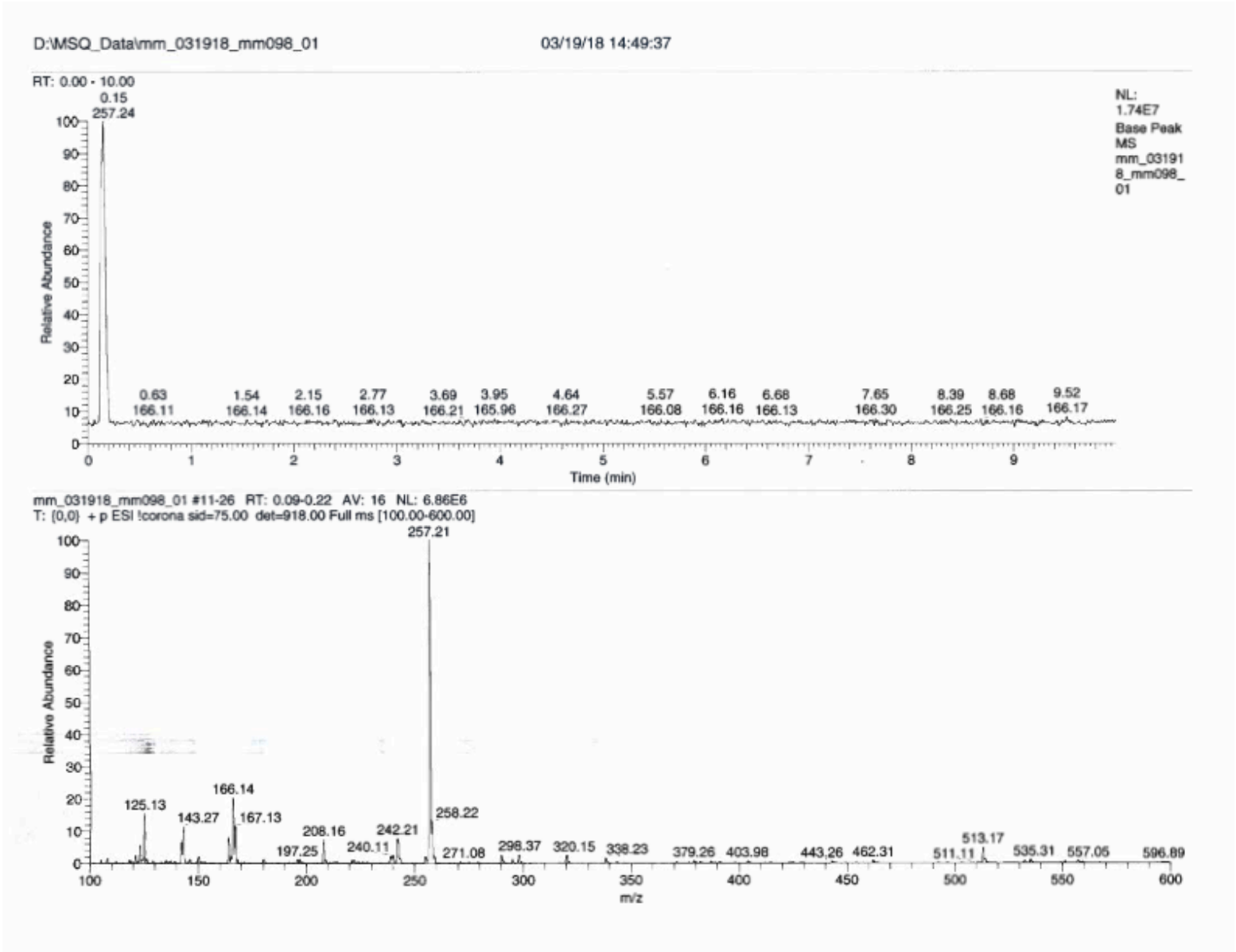



**Figure 28.** MS spectrum of NRH (**6a**) in 1:1 $H_2O$/ACN.

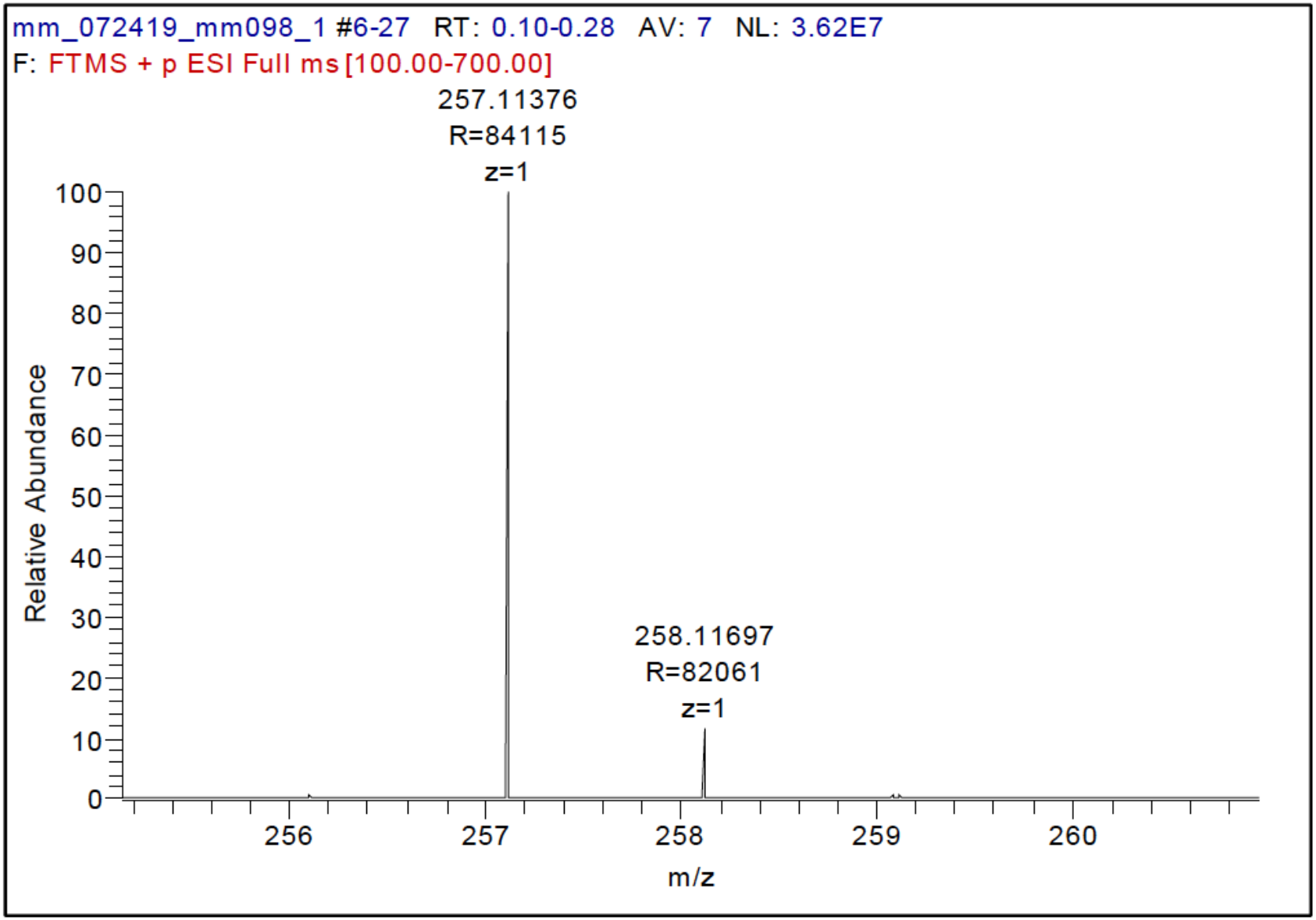



**Figure 29.** HRMS spectrum of NRH (**6a**) in 1:1 $H_2O$/ACN.

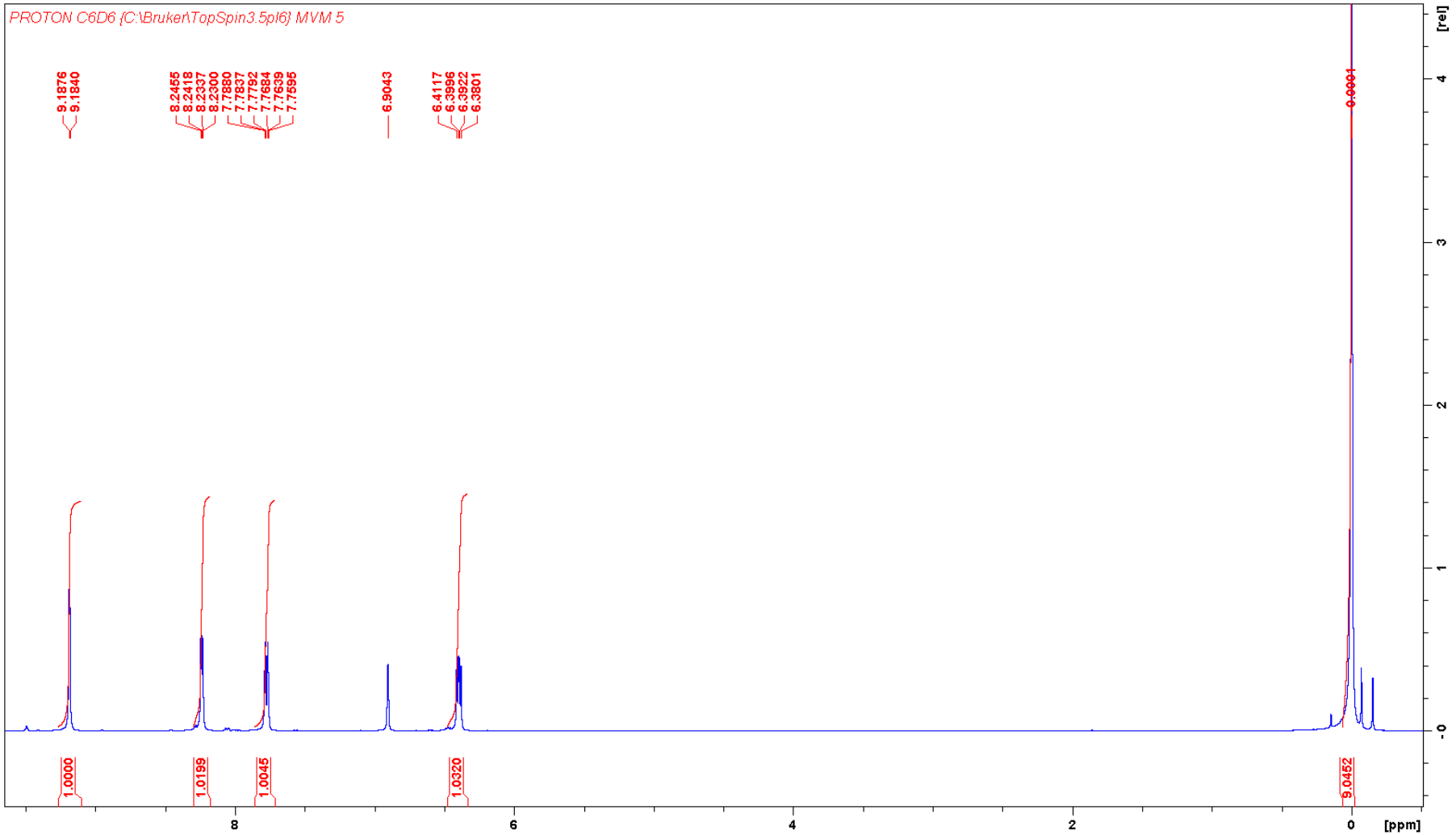



**Figure 30.** $^{1}$H NMR (benzene-$d_6$) of trimethylsilyl nicotinate (**2b**).

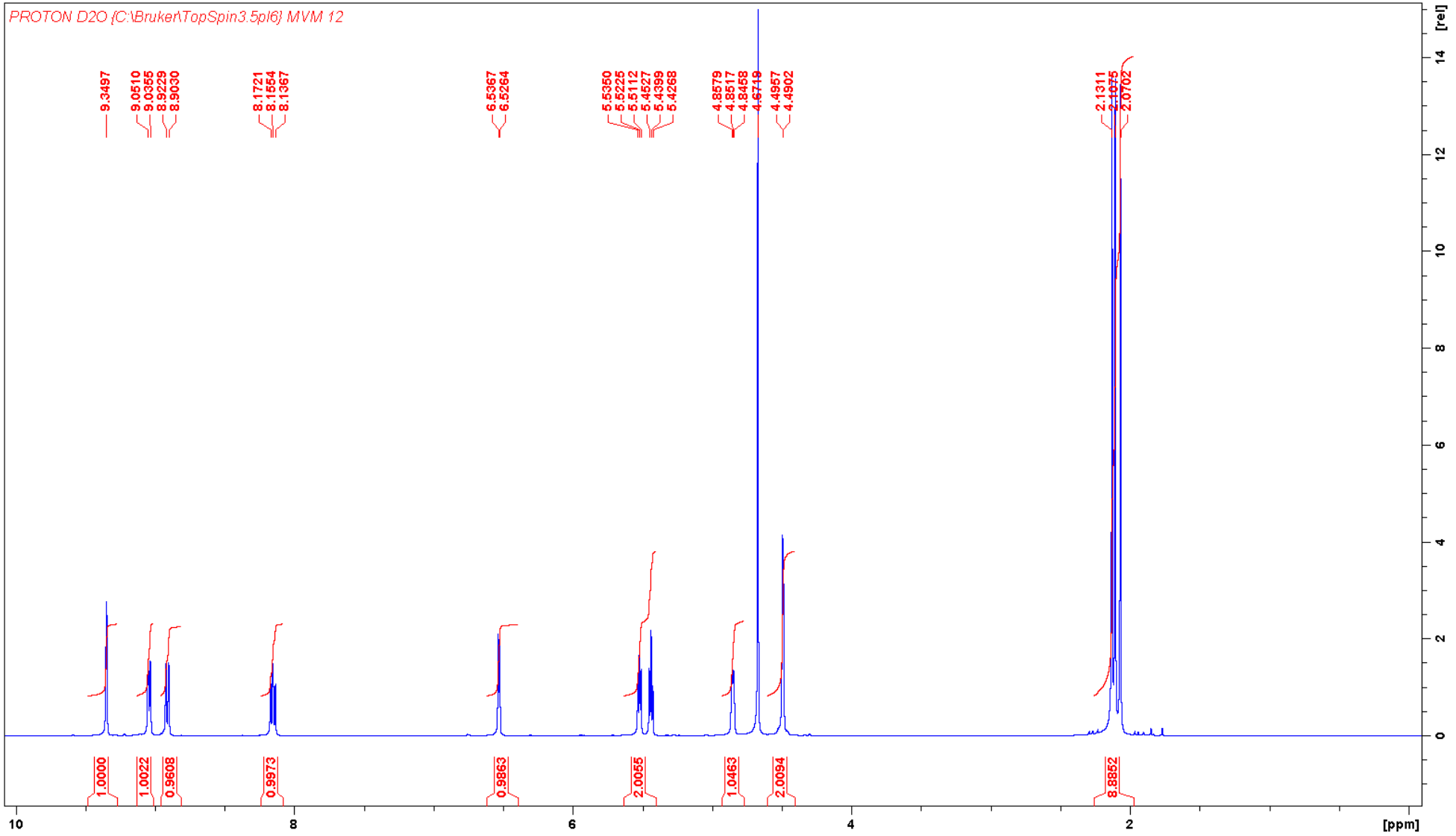



**Figure 31.** $^{1}H$ NMR ($D_2O$) of NAR TA (**3b**), general view.

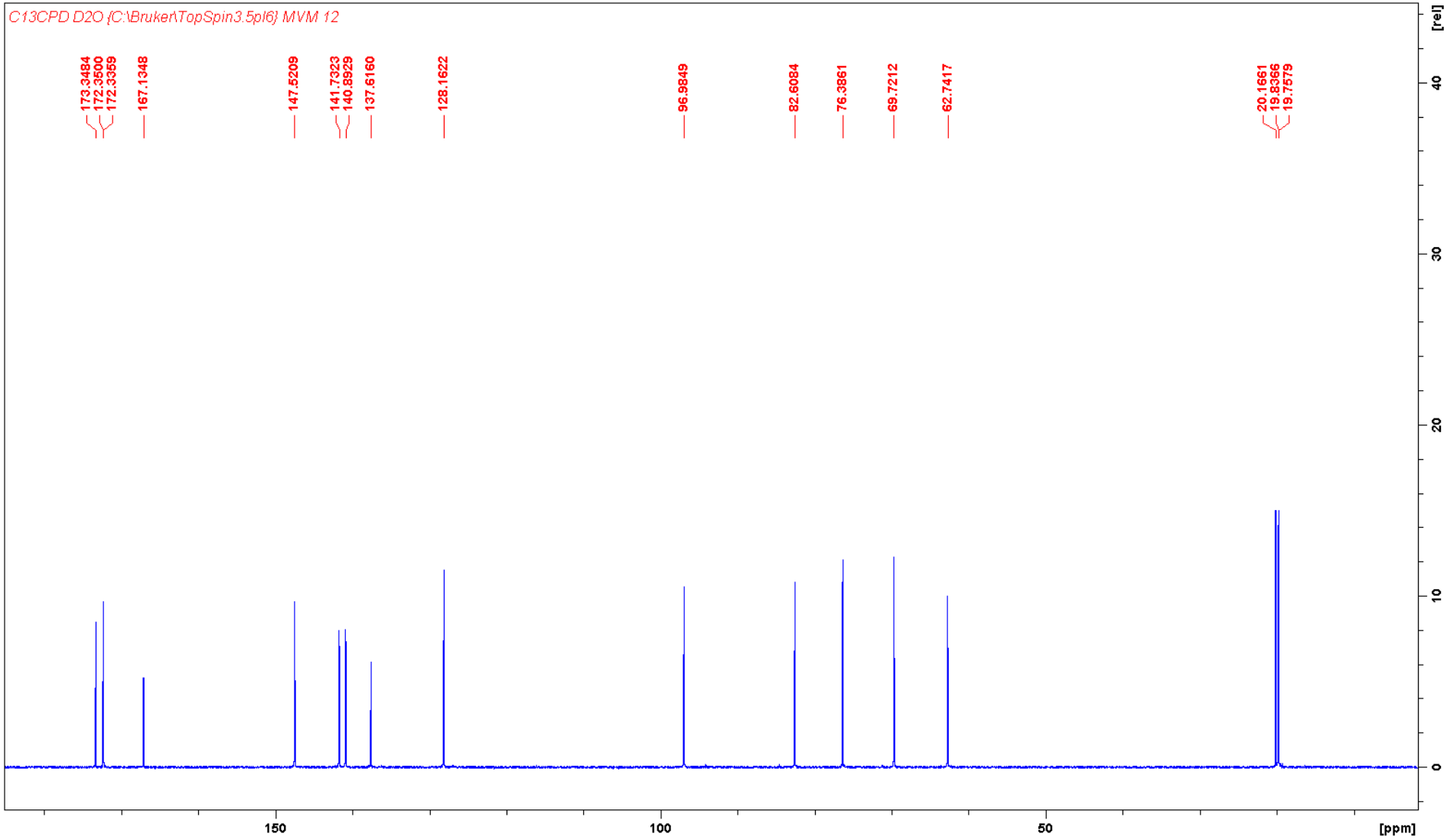



**Figure 32.** $^{13}C$ NMR ($D_2O$) of NAR TA (**3b**), general view.

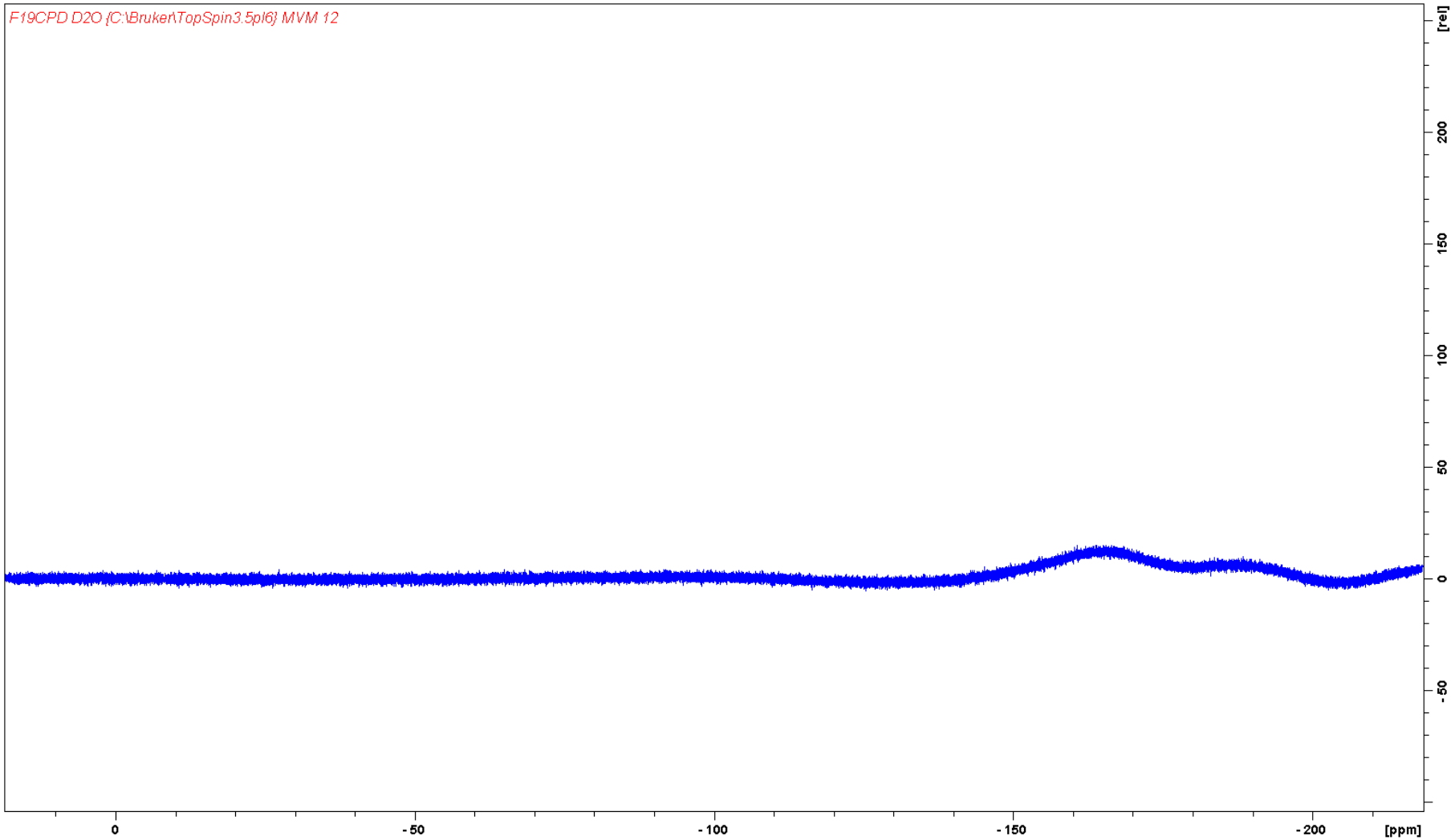



**Figure 33.** $^{19}F$ NMR ($D_2O$) of NAR TA (**3b**), general view.

COSY ($D_2O$) of NAR TA (**8**)

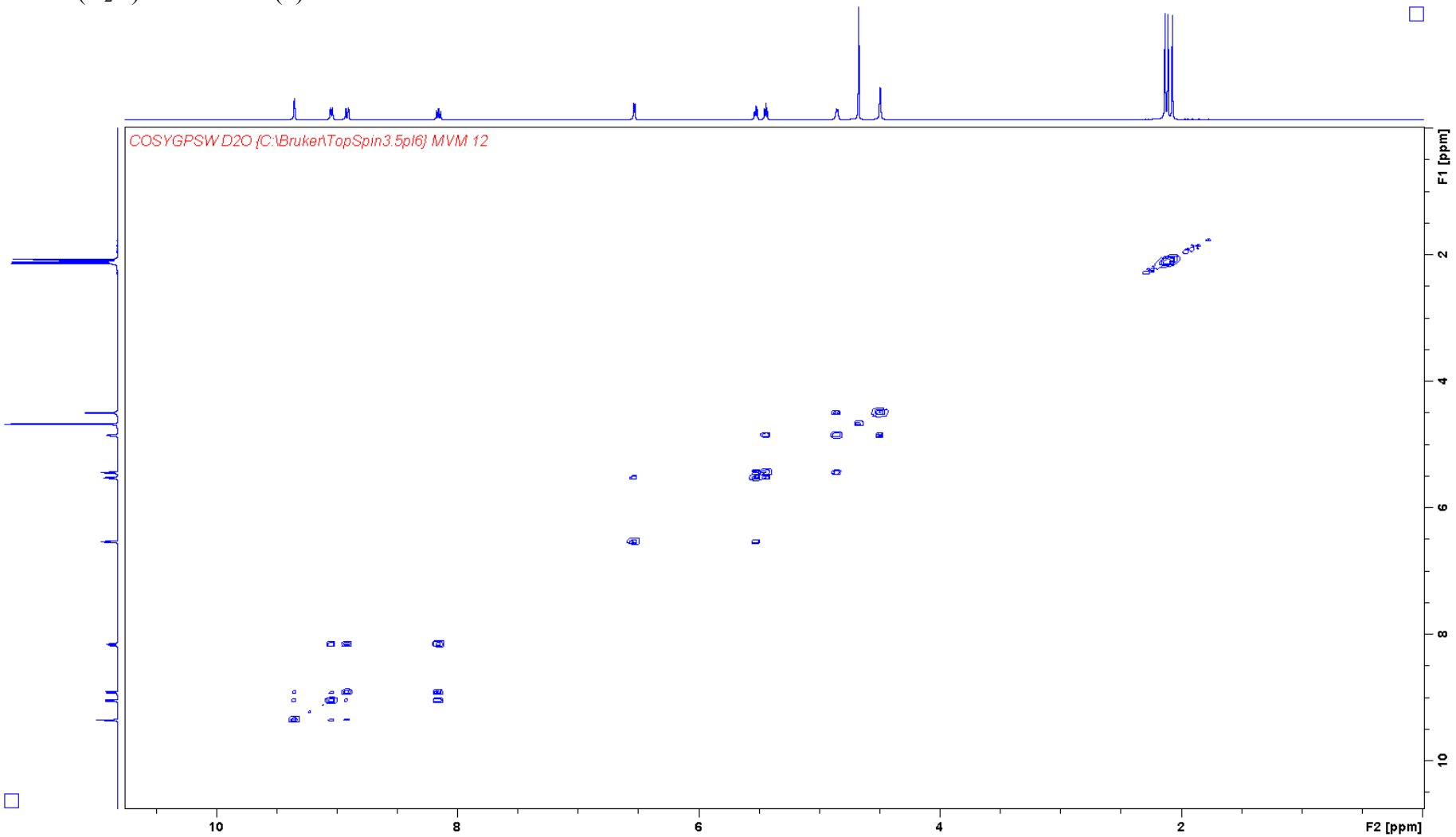



**Figure 34.** COSY ($D_2O$) of NAR TA (**3b**).

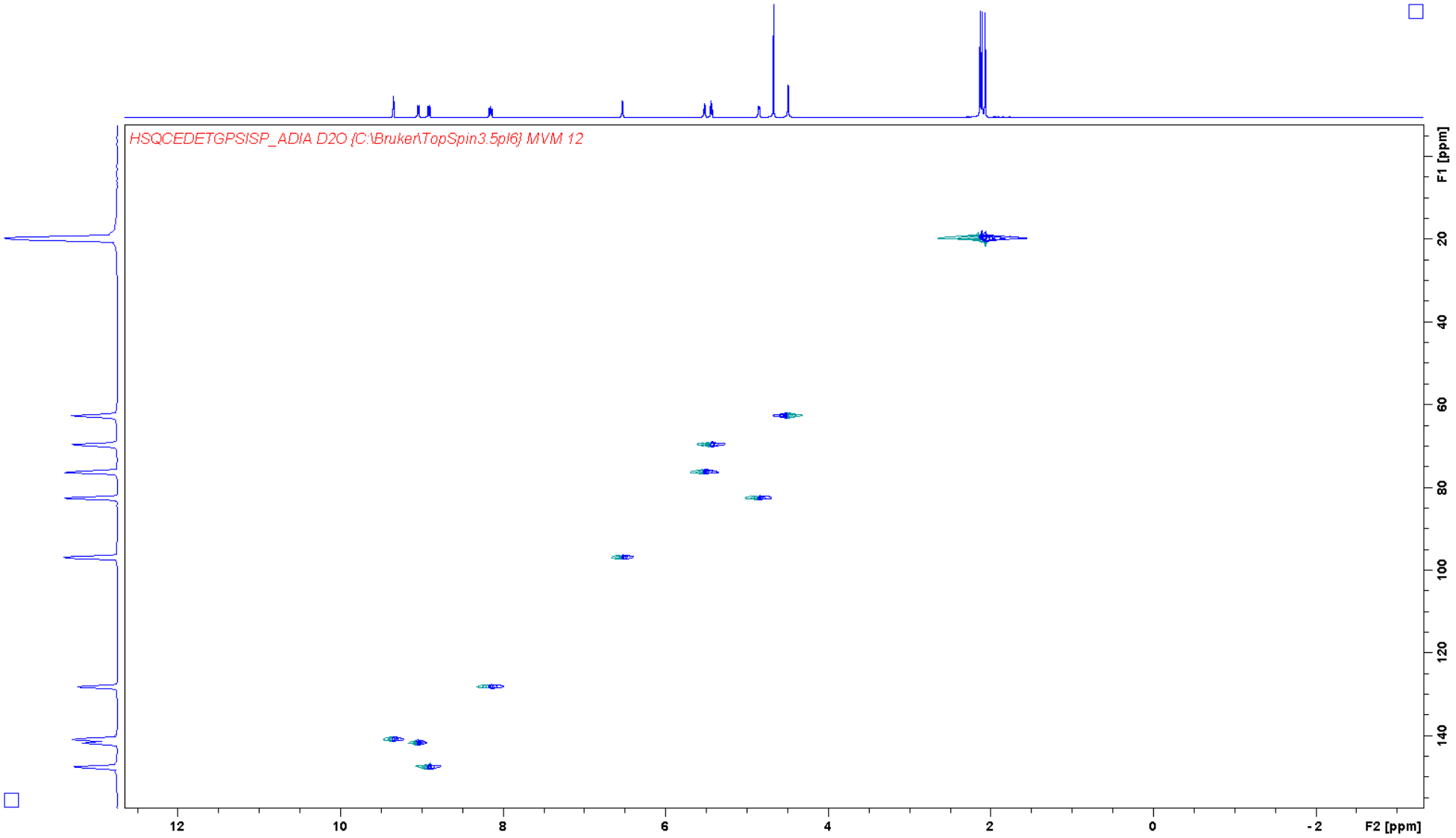



**Figure 35.** HSQC ($D_2O$) of NAR TA (**3b**).

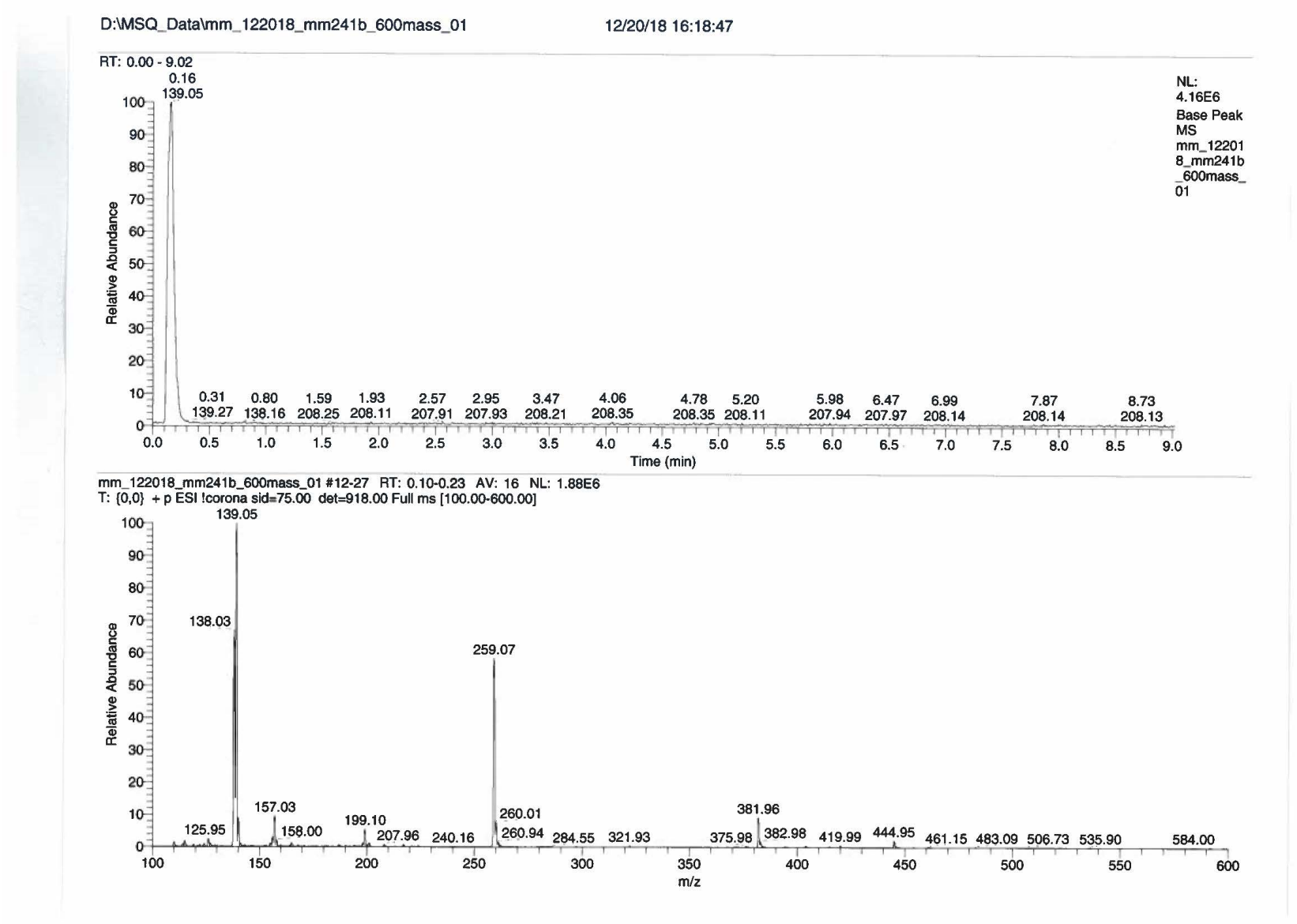



**Figure 36.** MS spectrum of NAR TA (**3b**) in 1:1 $H_2O$/ACN.

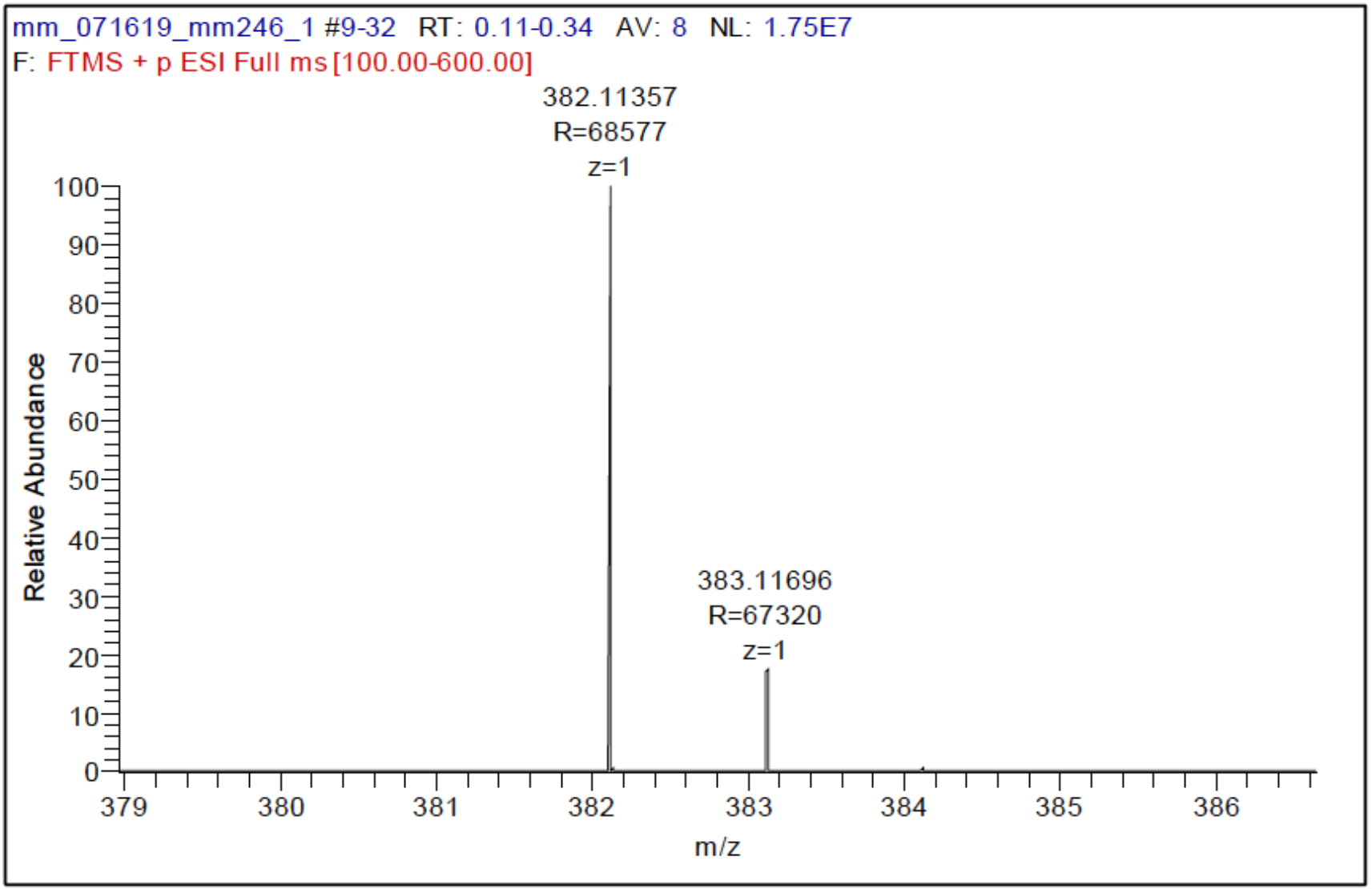



**Figure 37.** HRMS spectrum of NAR TA (**3b**) in 1:1 $H_2O$/ACN.

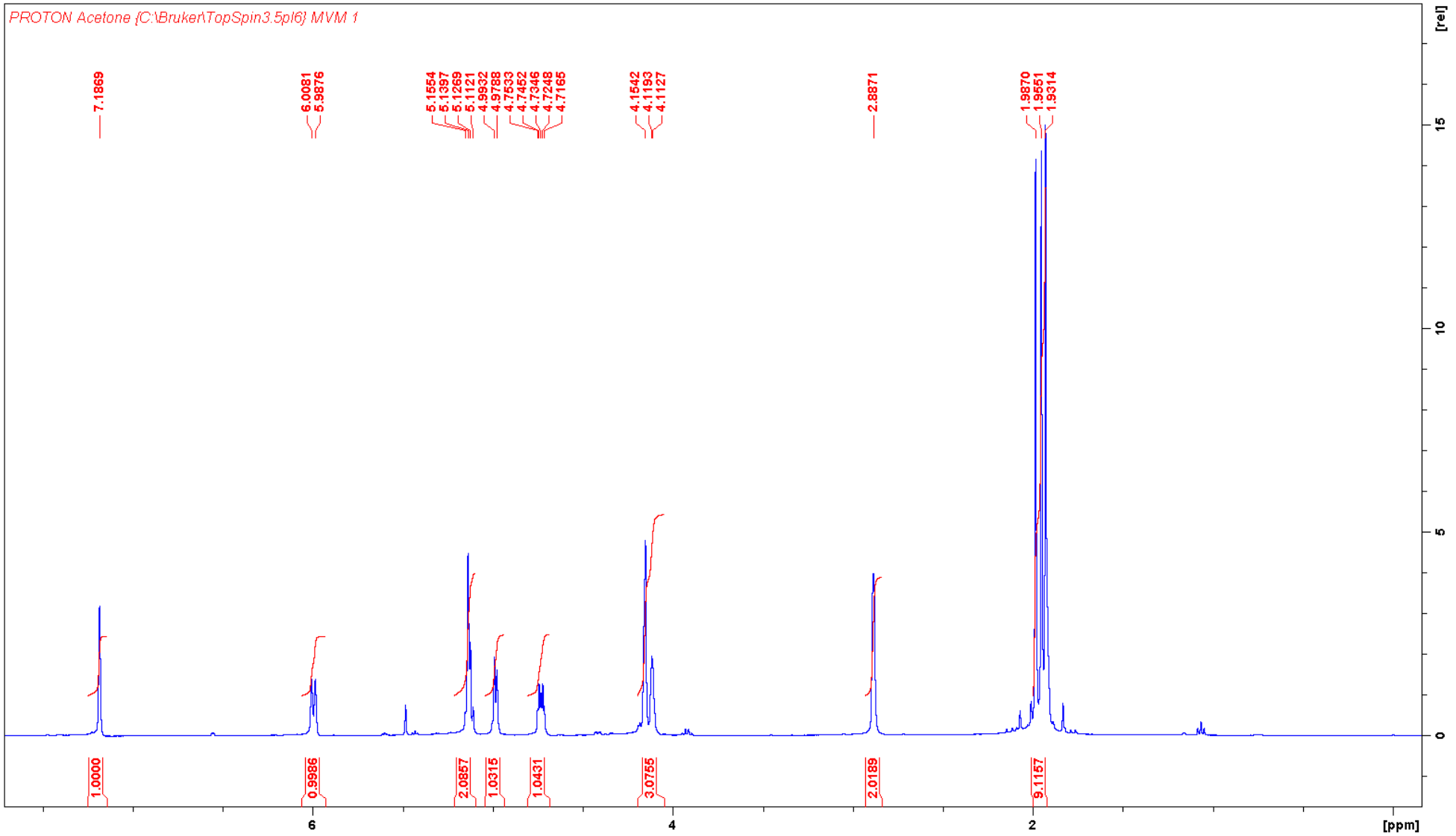



**Figure 38.** $^{1}H$ NMR ($D_2O$) of NARH TA (**4b**), general view.

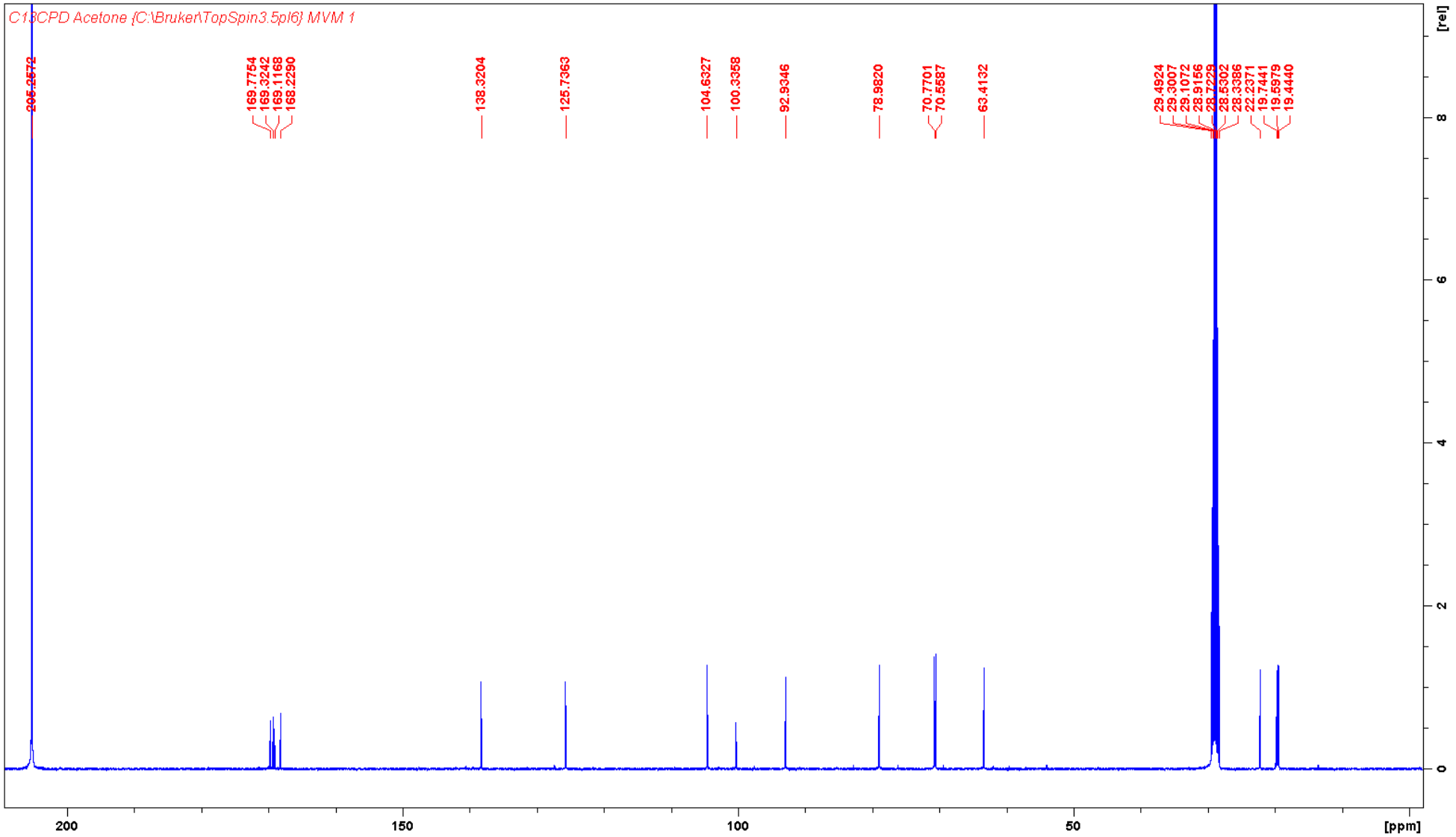



**Figure 39.** $^{13}C$ NMR ($D_2O$) of NARH TA (**4b**).

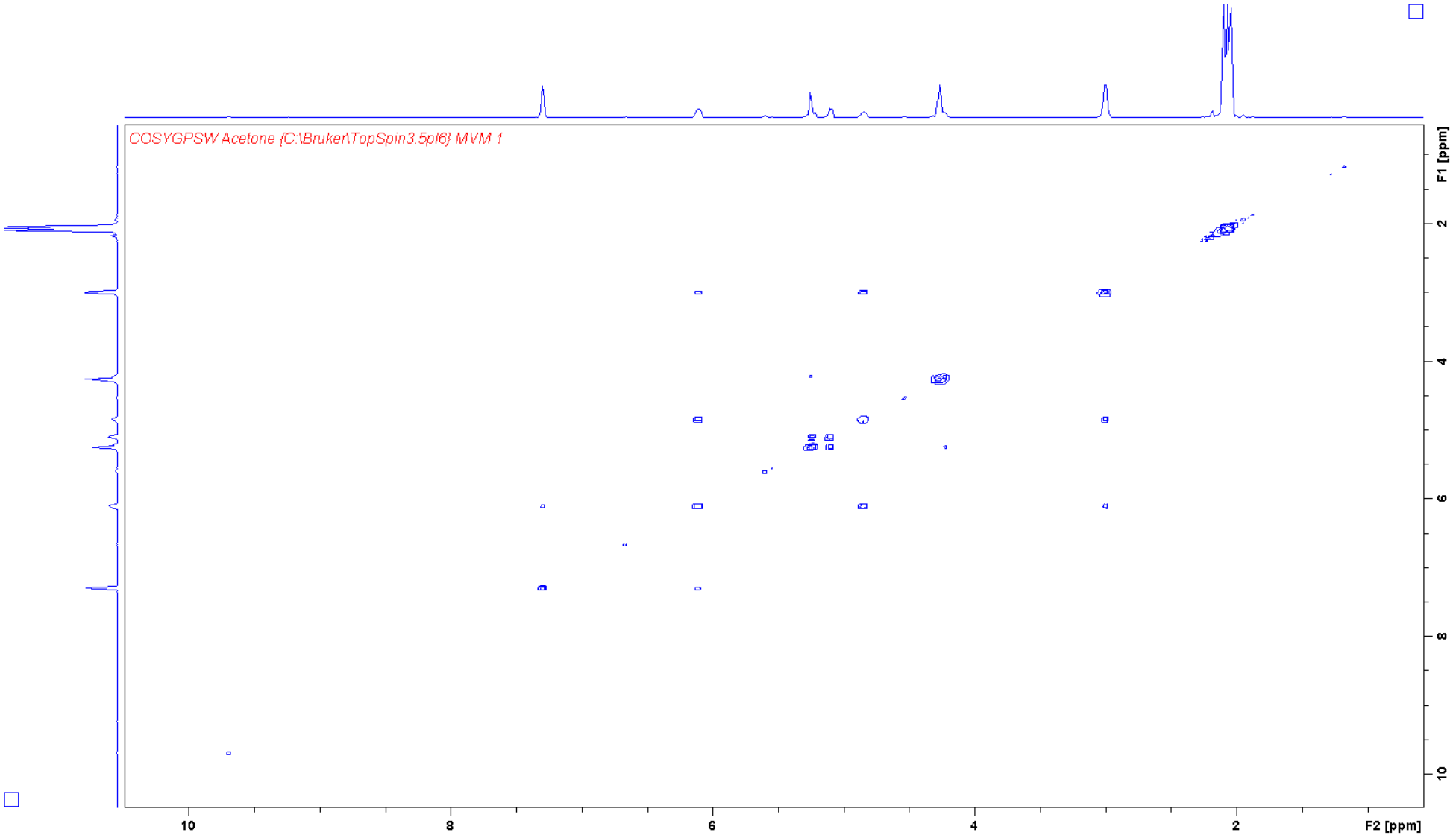



**Figure 40.** COSY ($D_2O$) of NARH TA (**4b**).

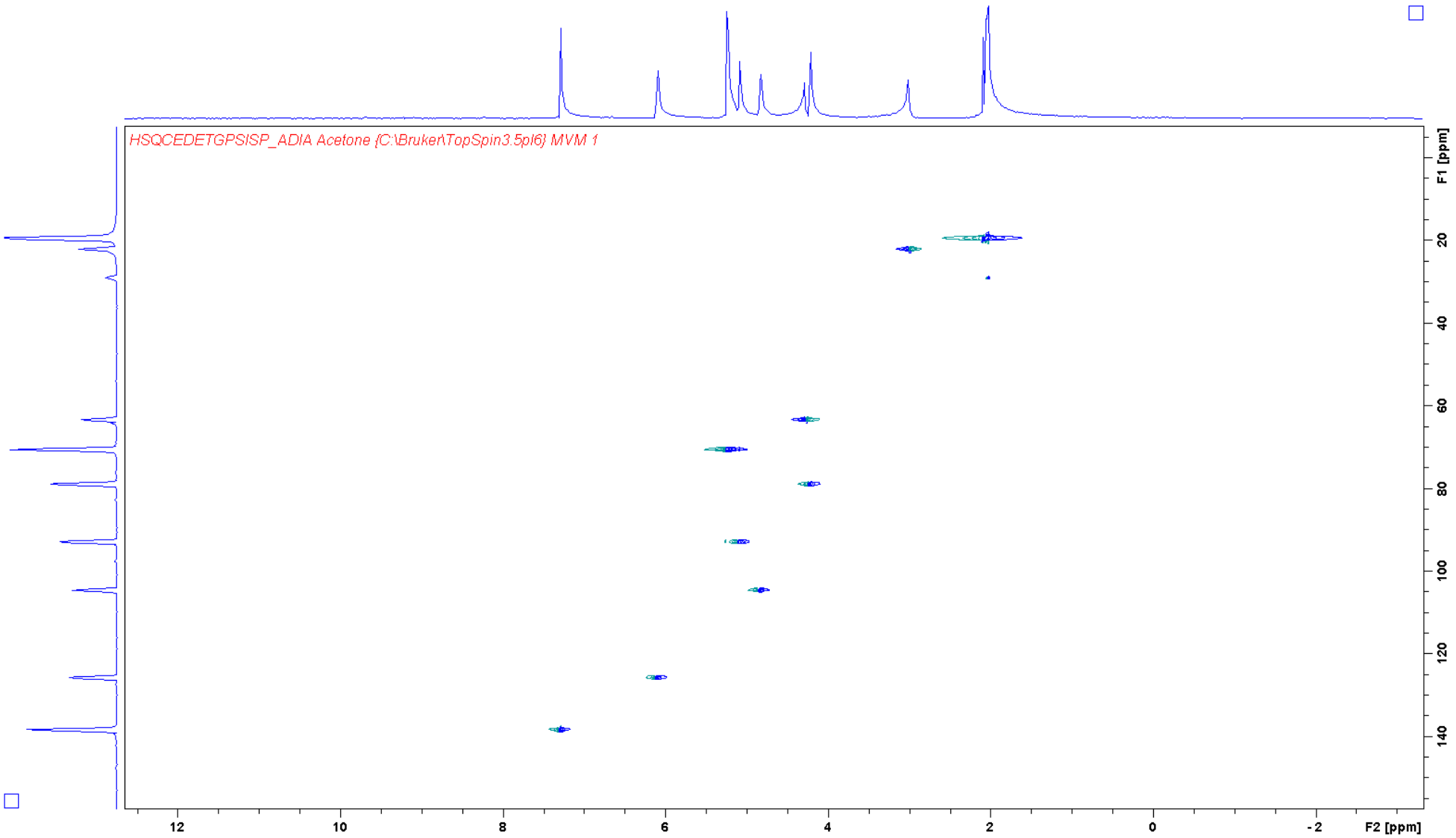



**Figure 41.** HSQC ($D_2O$) of NARH TA (**4b**).

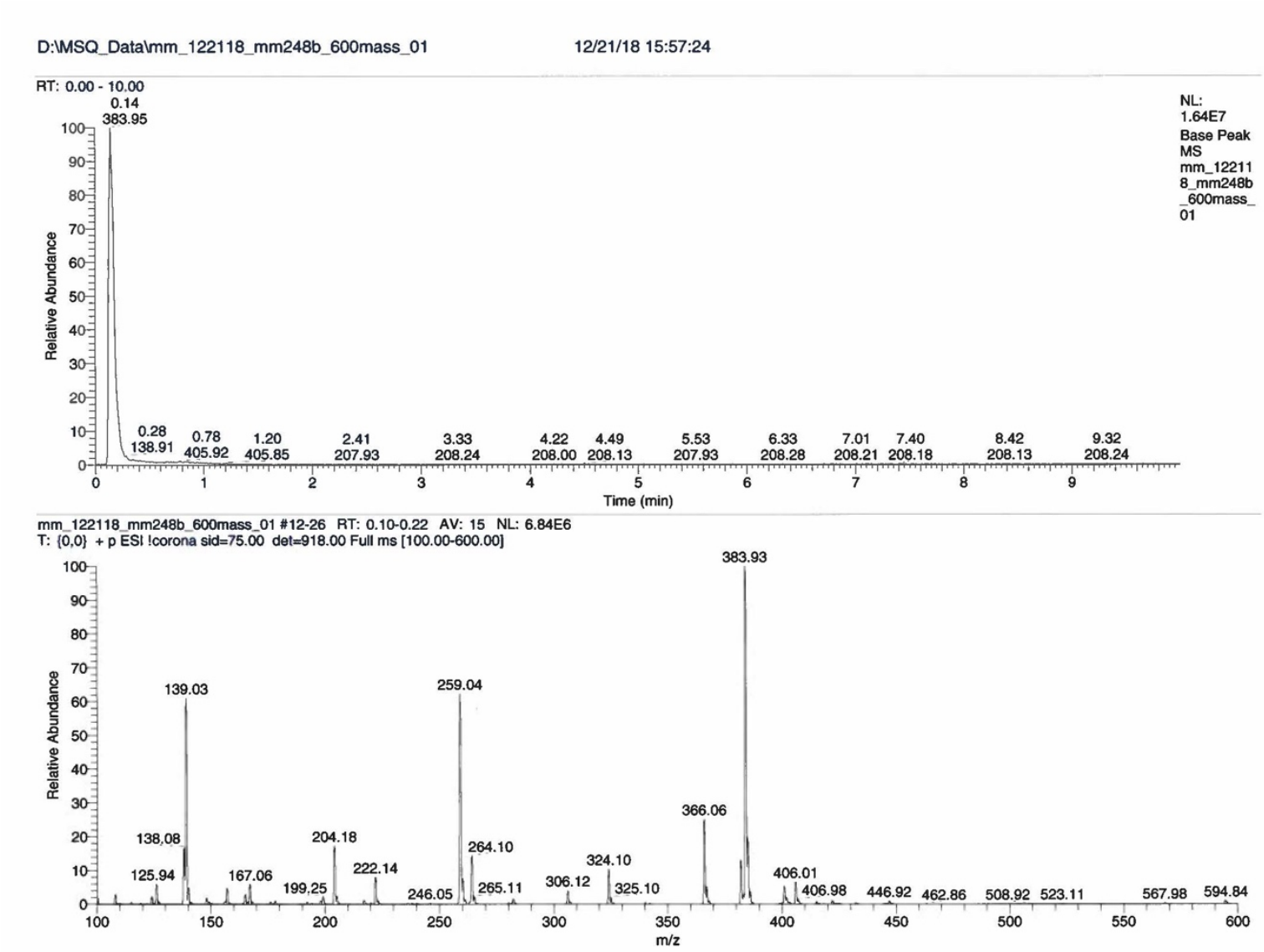



**Figure 42.** MS spectrum of NARH TA (**4b**) in 1:1 $H_2O$/ACN.

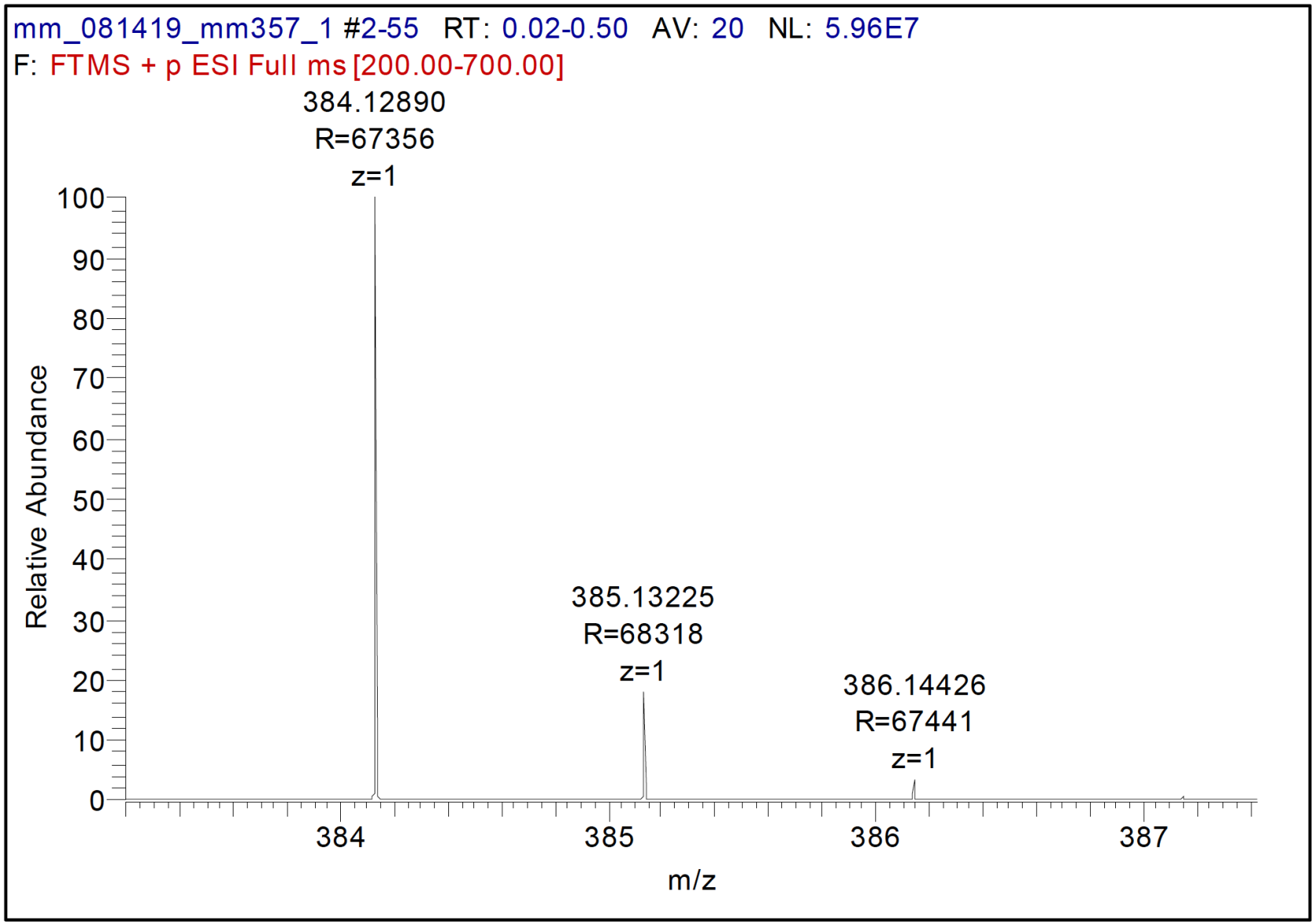



**Figure 43.** HRMS spectrum of NARH TA (**4b**) in 1:1 $H_2O$/ACN.

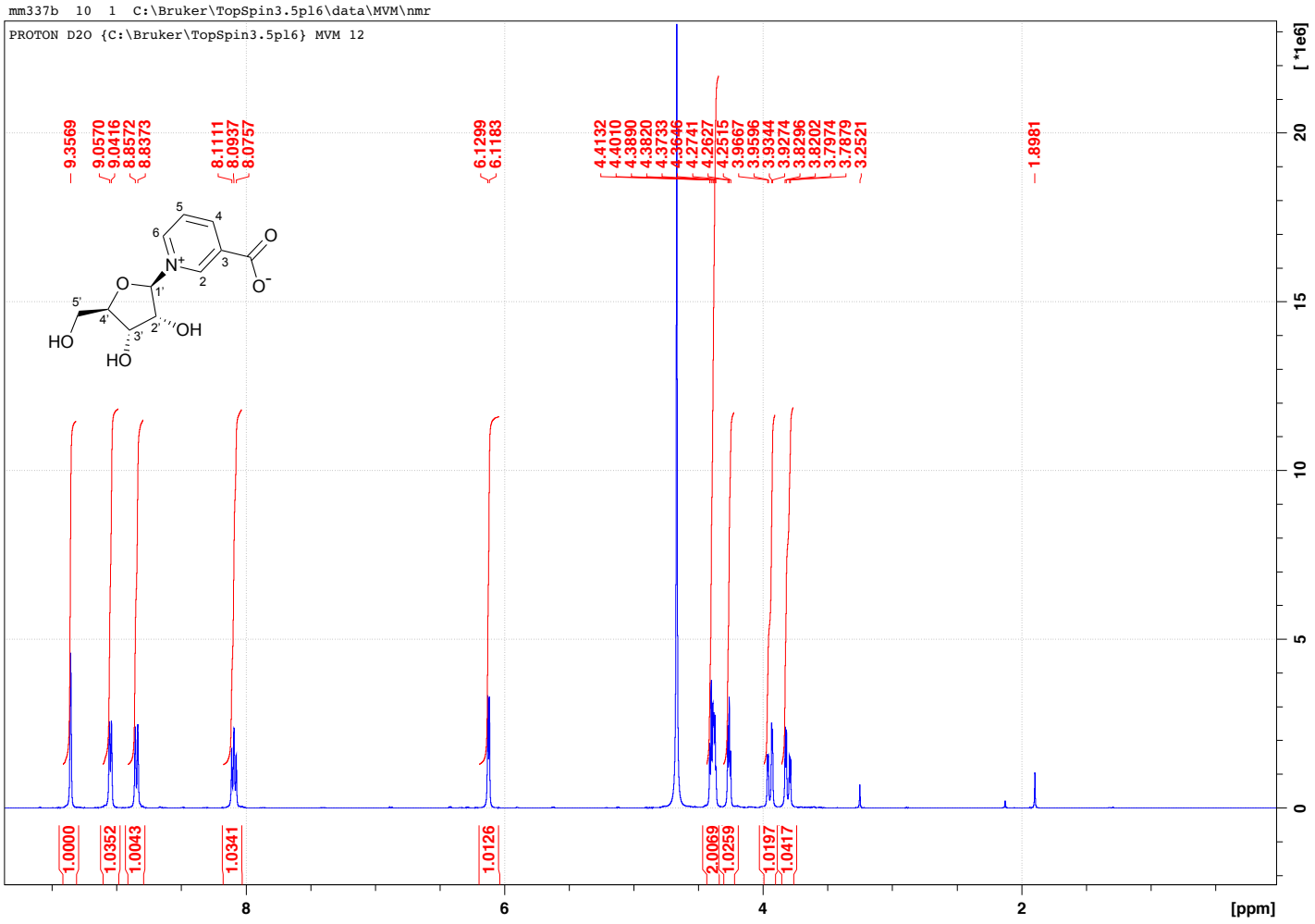



**Figure 44.** $^{1}H$ NMR ($D_2O$) of NAR (**5b**), general view.

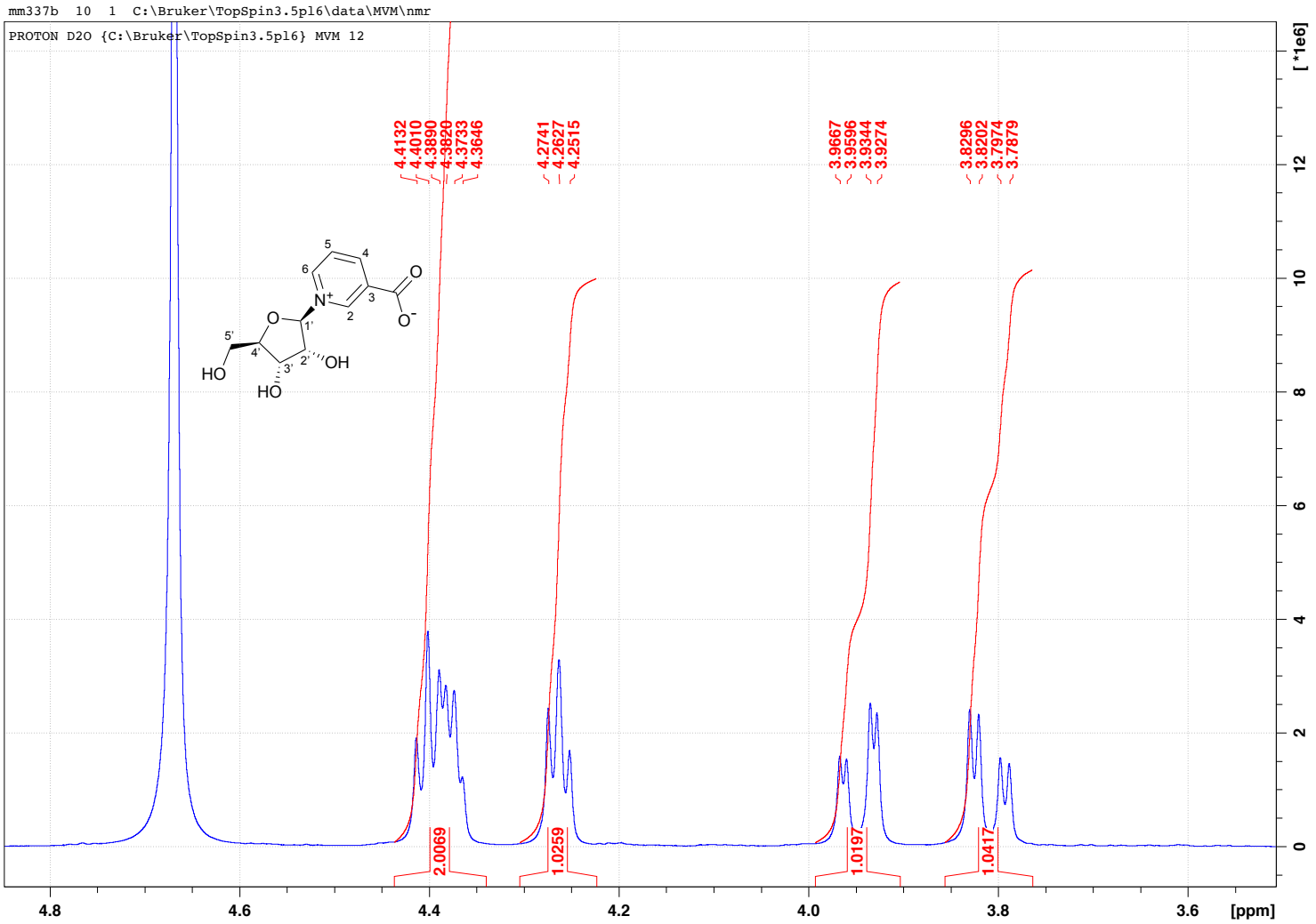



**Figure 45.** $^{1}H$ NMR ($D_2O$) of NAR (**5b**), zoomed from 3.6 to 4.8 ppm.

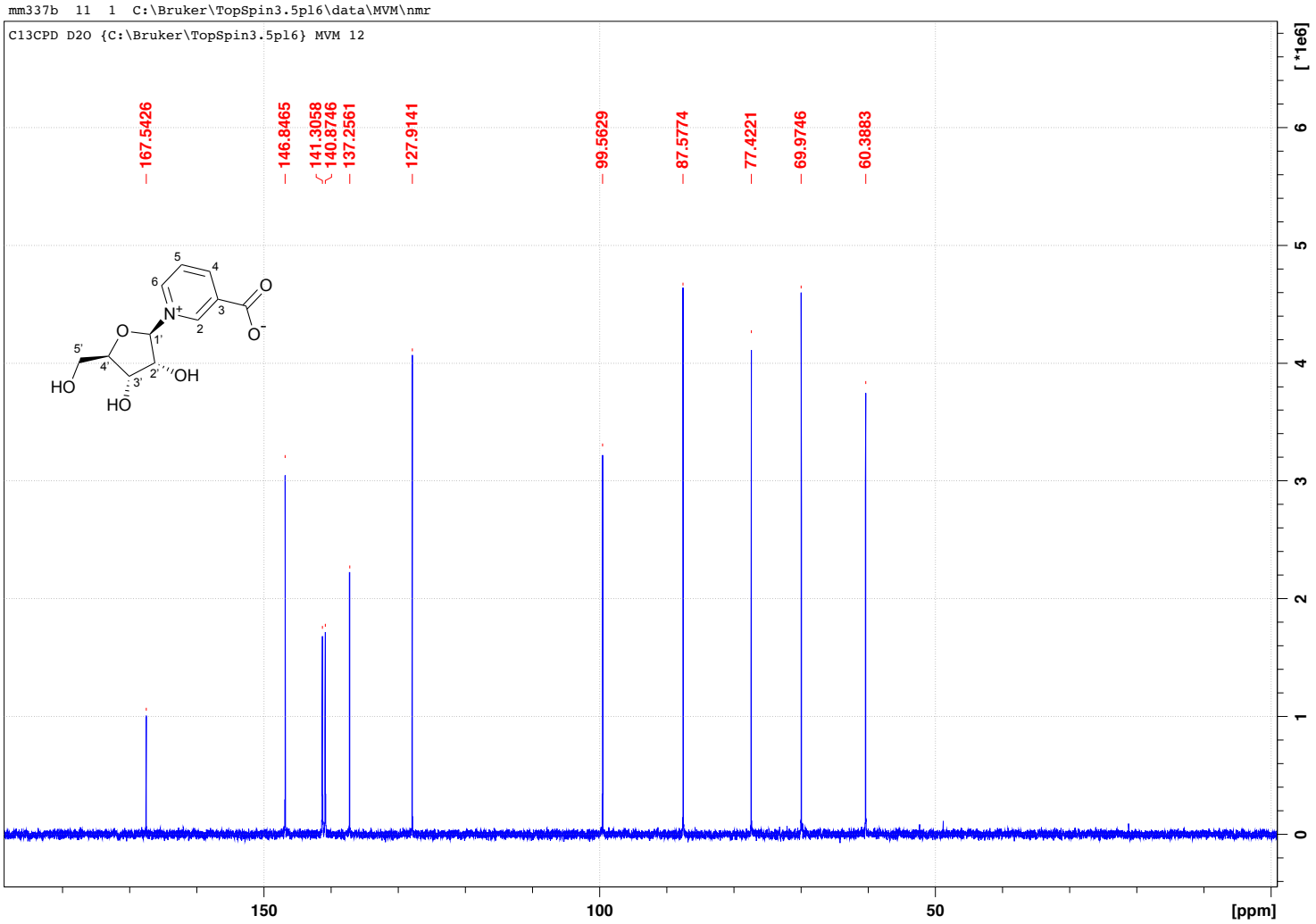



**Figure 46.** $^{13}C$ NMR ($D_2O$) of NAR (**5b**), general view.

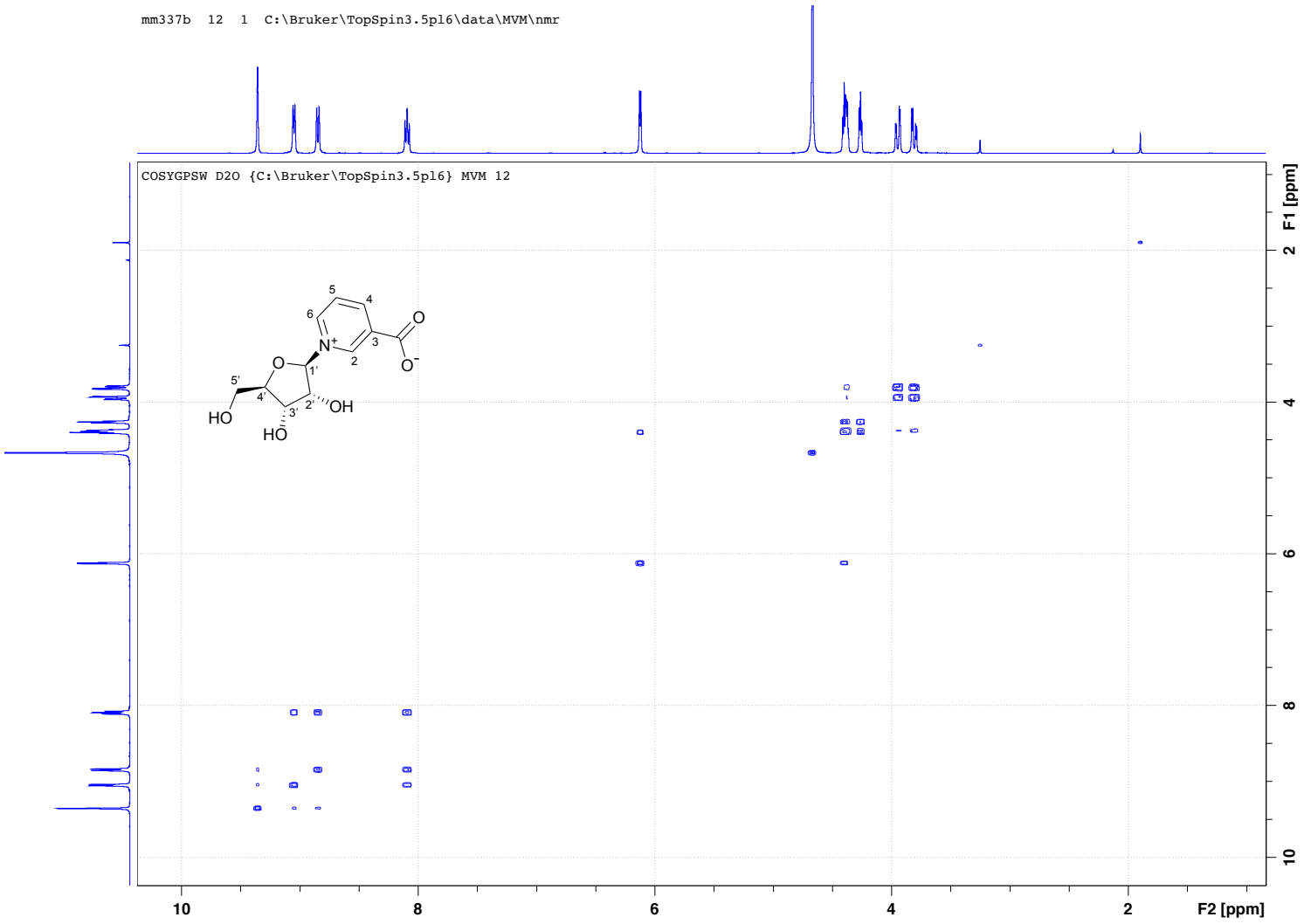



**Figure 47.** COSY ($D_2O$) of NAR (**5b**).

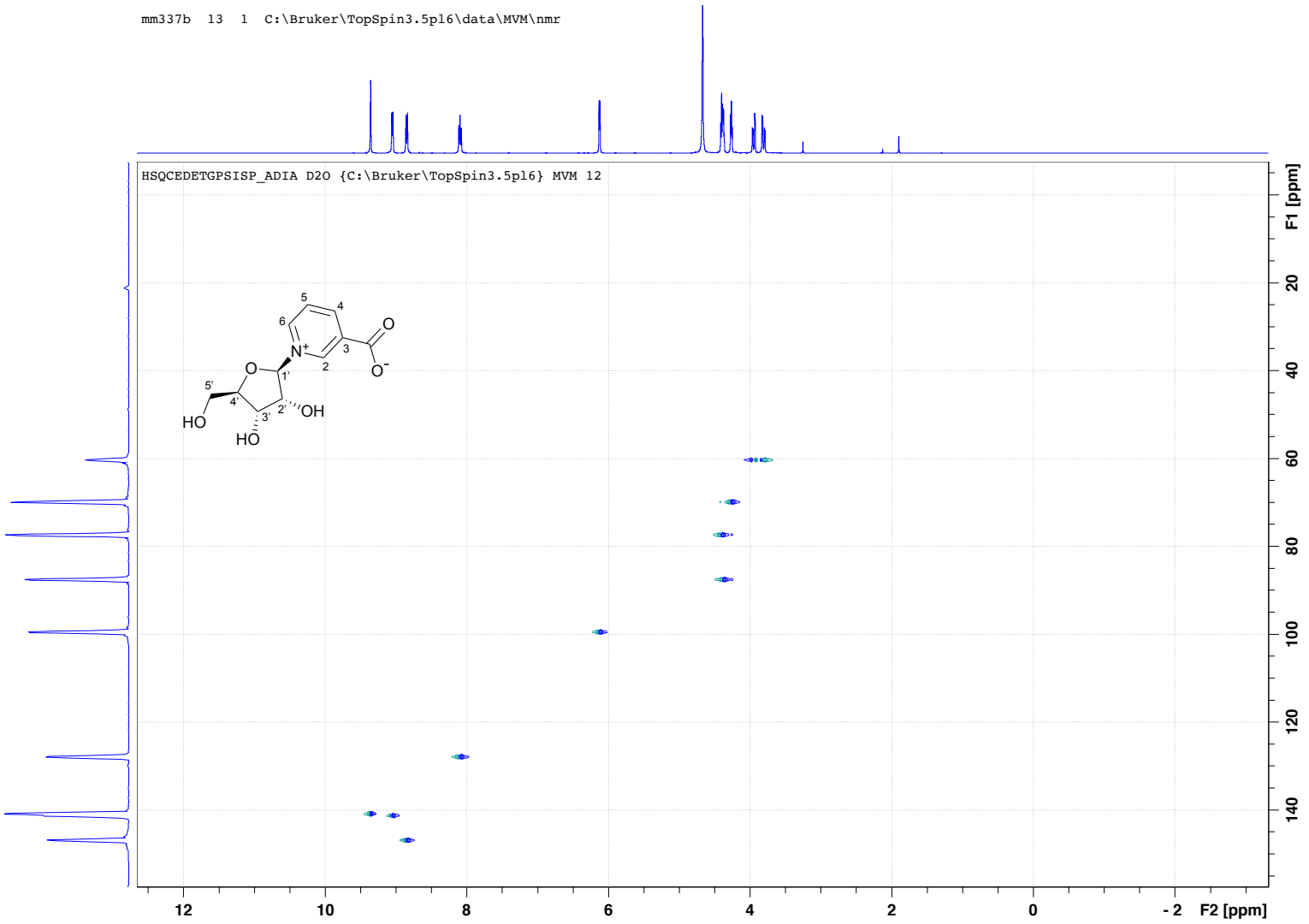



**Figure 48.** HSQC ($D_2O$) of NAR (**5b**).

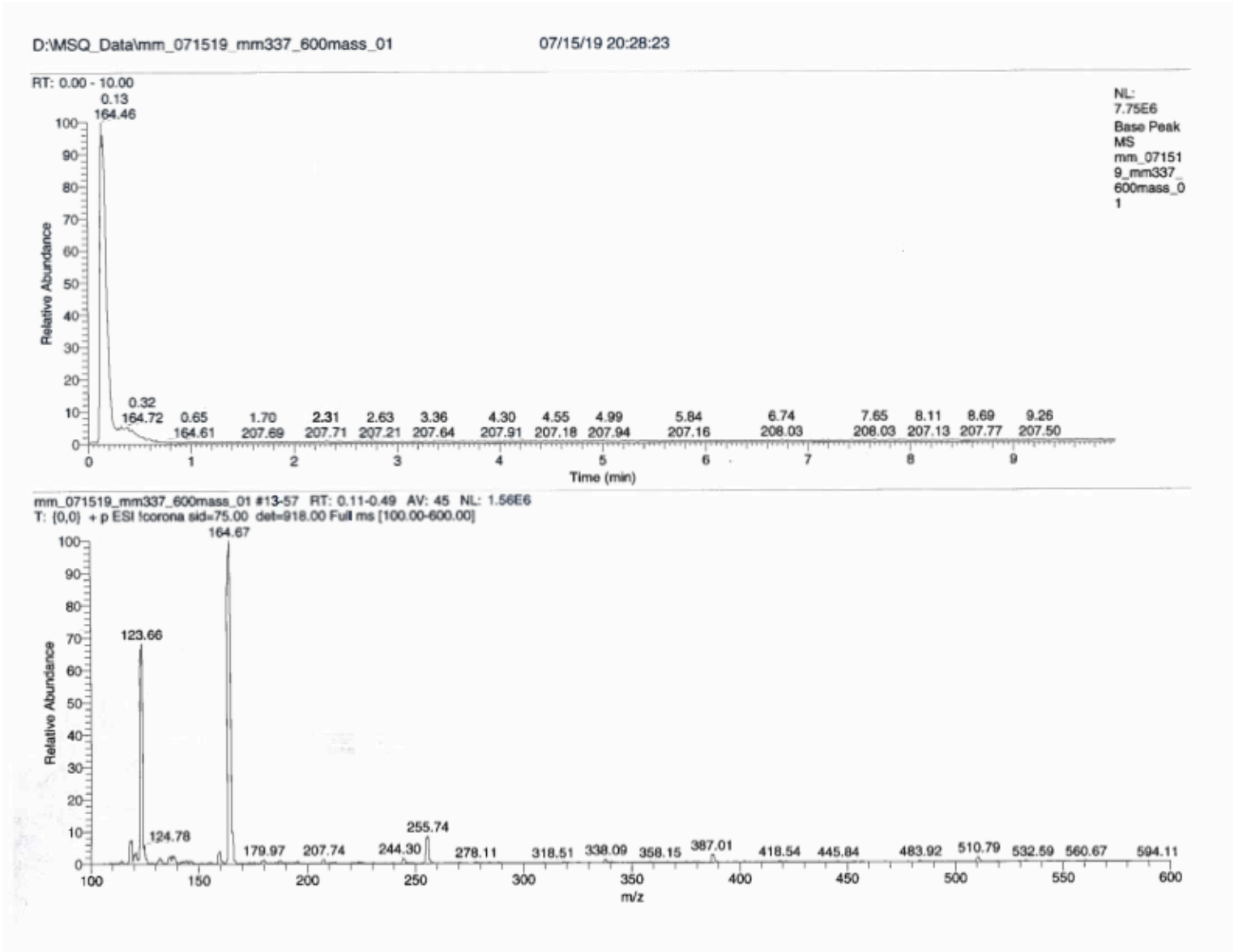



**Figure 49.** MS spectrum of NAR (**5b**) in 1:1 $H_2O$/ACN.

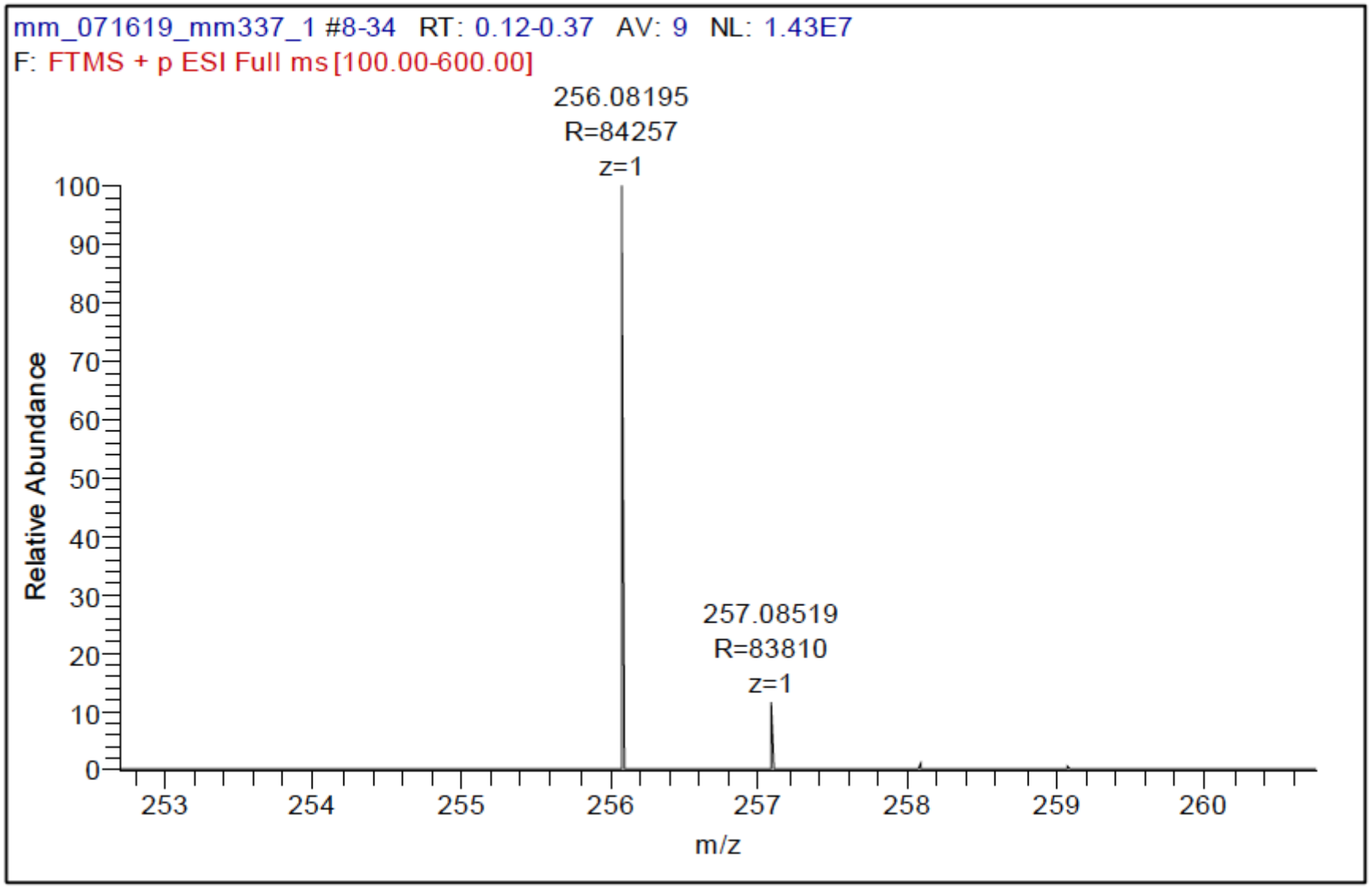



**Figure 50.** HRMS spectrum of NAR (**5b**) in 1:1 $H_2O$/ACN.

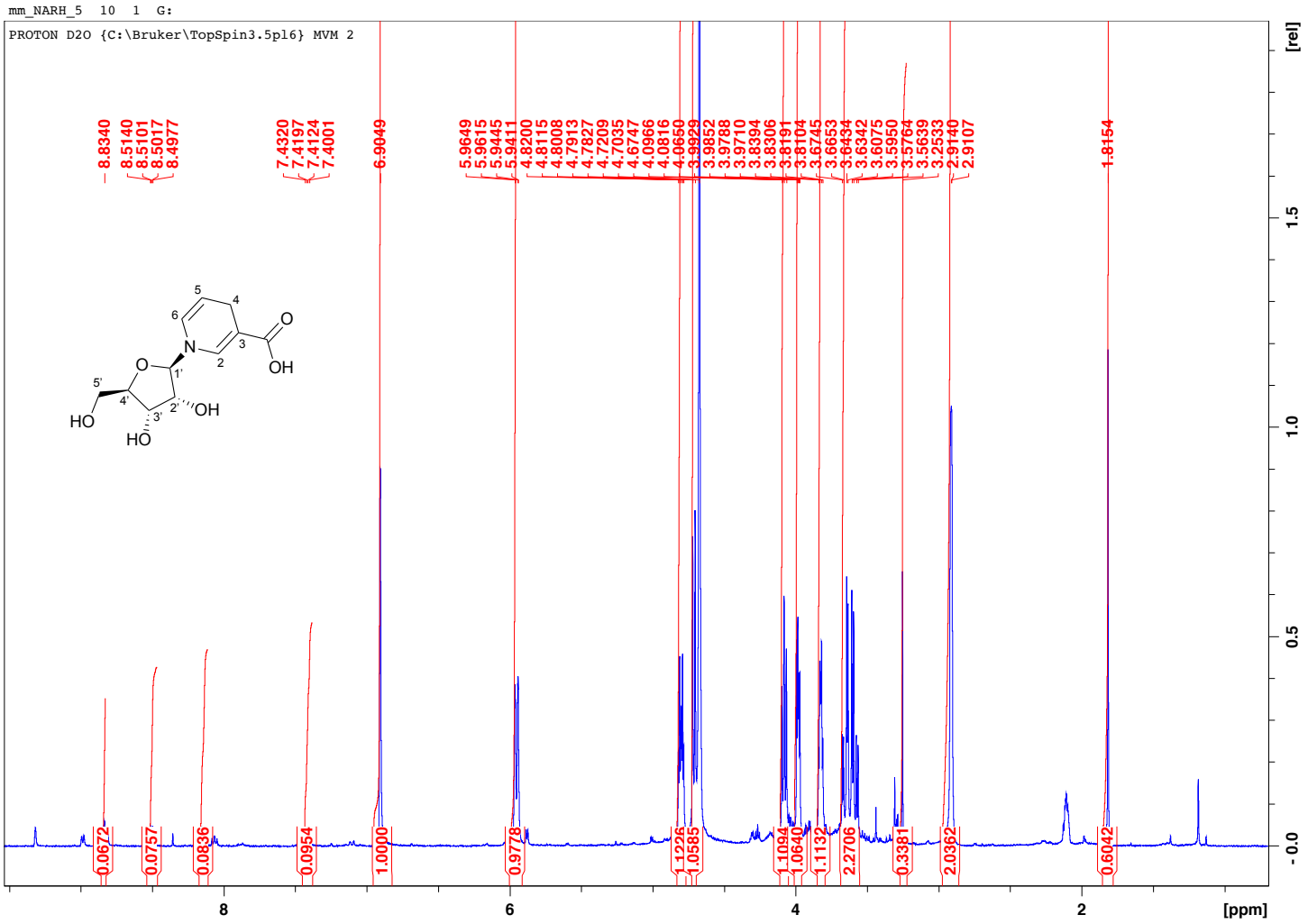



**Figure 51.** $^{1}H$ NMR ($D_2O$) of NARH (**6b**), general view.

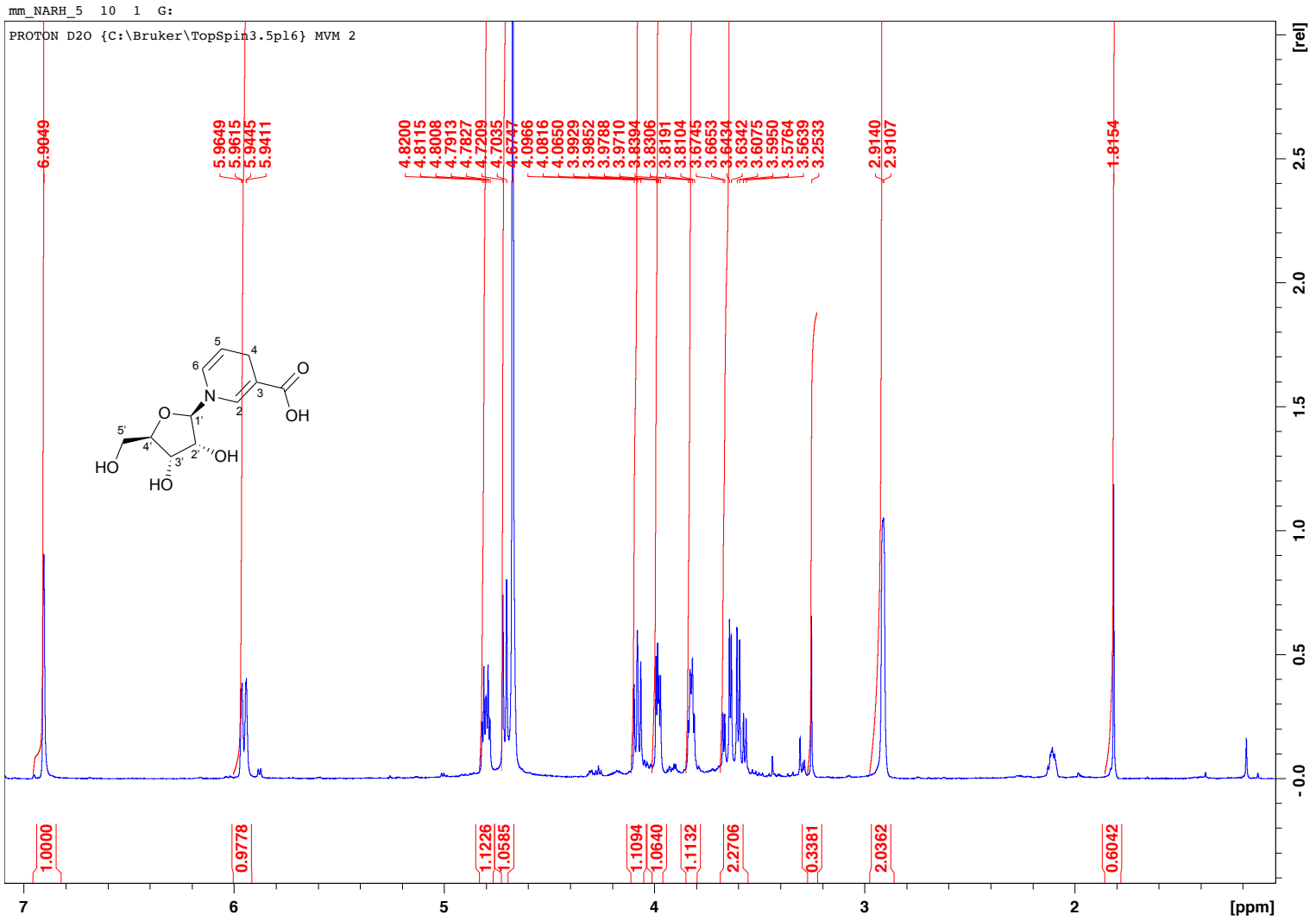



**Figure 52.** $^{1}H$ NMR ($D_2O$) of NARH (**6b**), zoomed from 1.2 to 7.0 ppm.

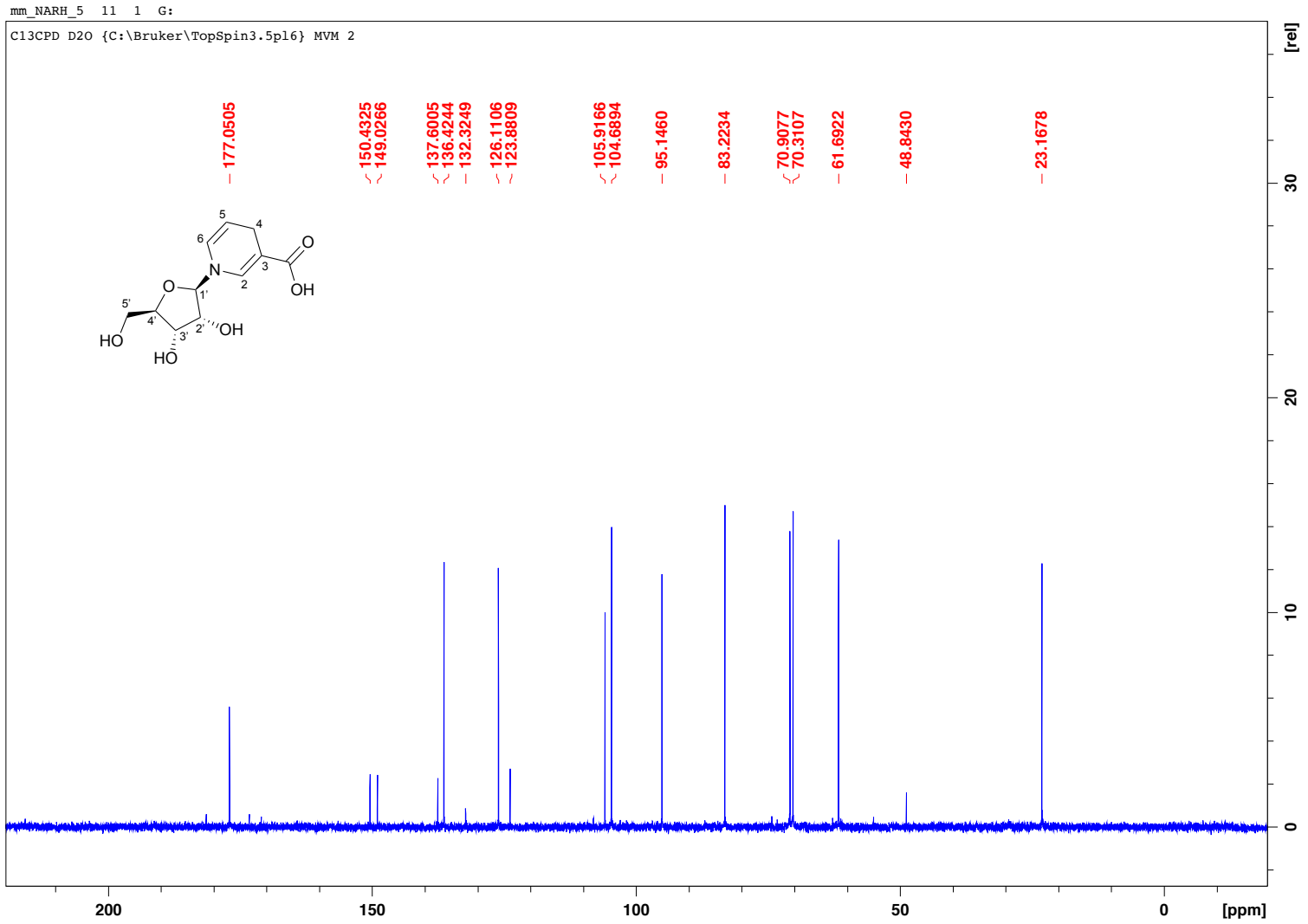



**Figure 53.** $^{13}C$ NMR ($D_2O$) of NARH (**6b**), general view.

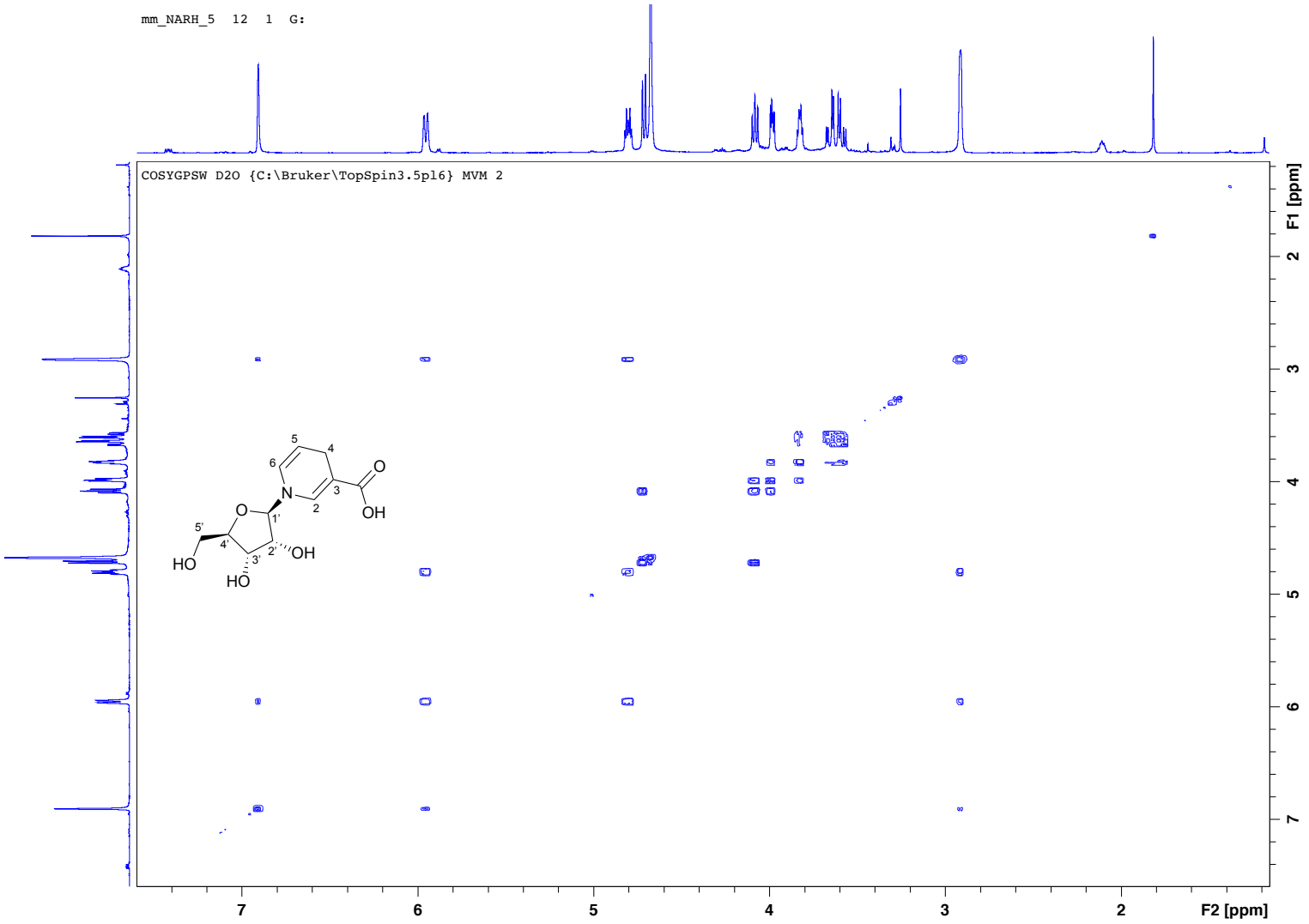



**Figure 54.** COSY ($D_2O$) of NARH (**6b**).

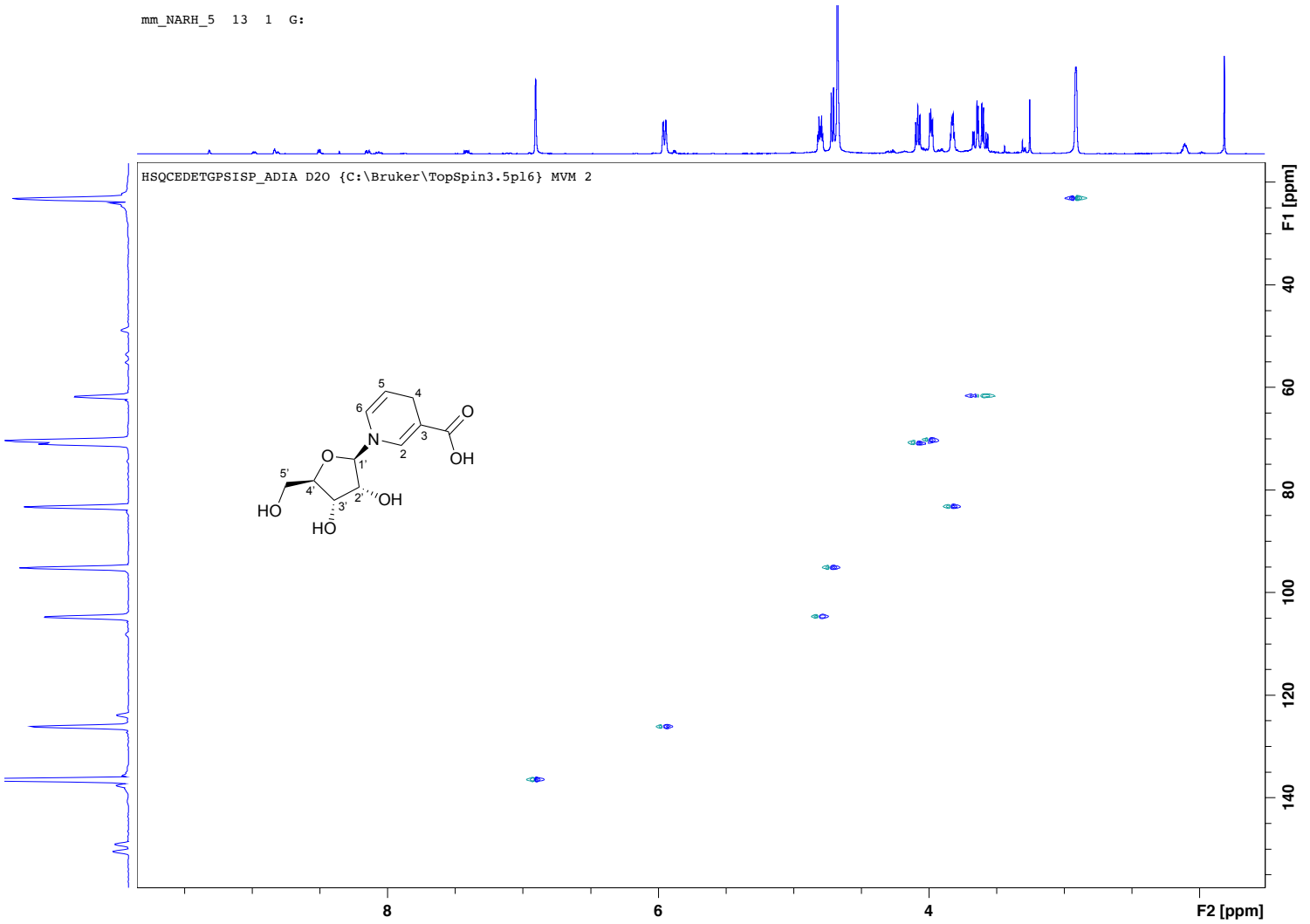



**Figure 55.** HSQC ($D_2O$) of NARH (**6b**).

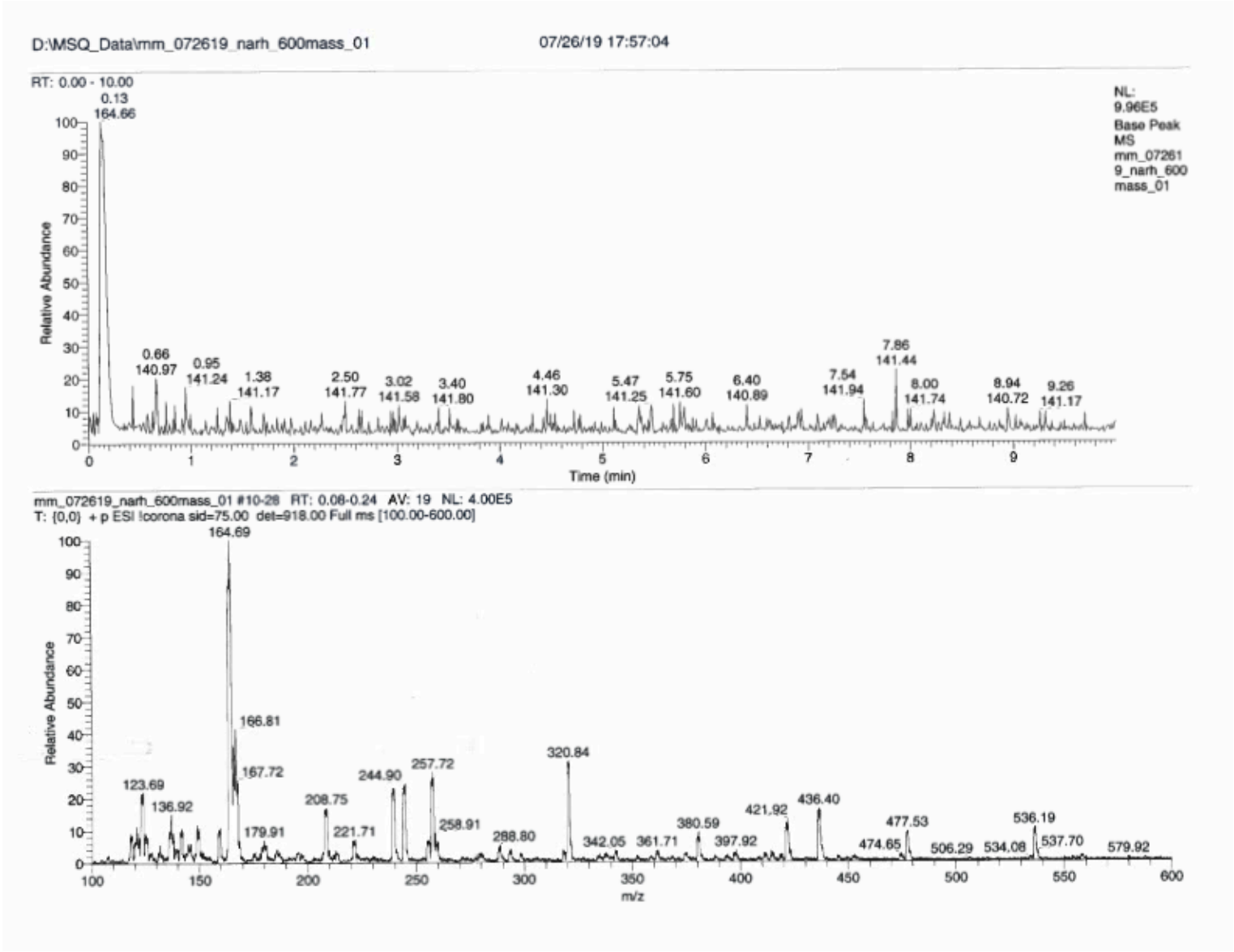



**Figure 56.** MS of NARH (**6b**) in 1:1 $H_2O$/ACN.

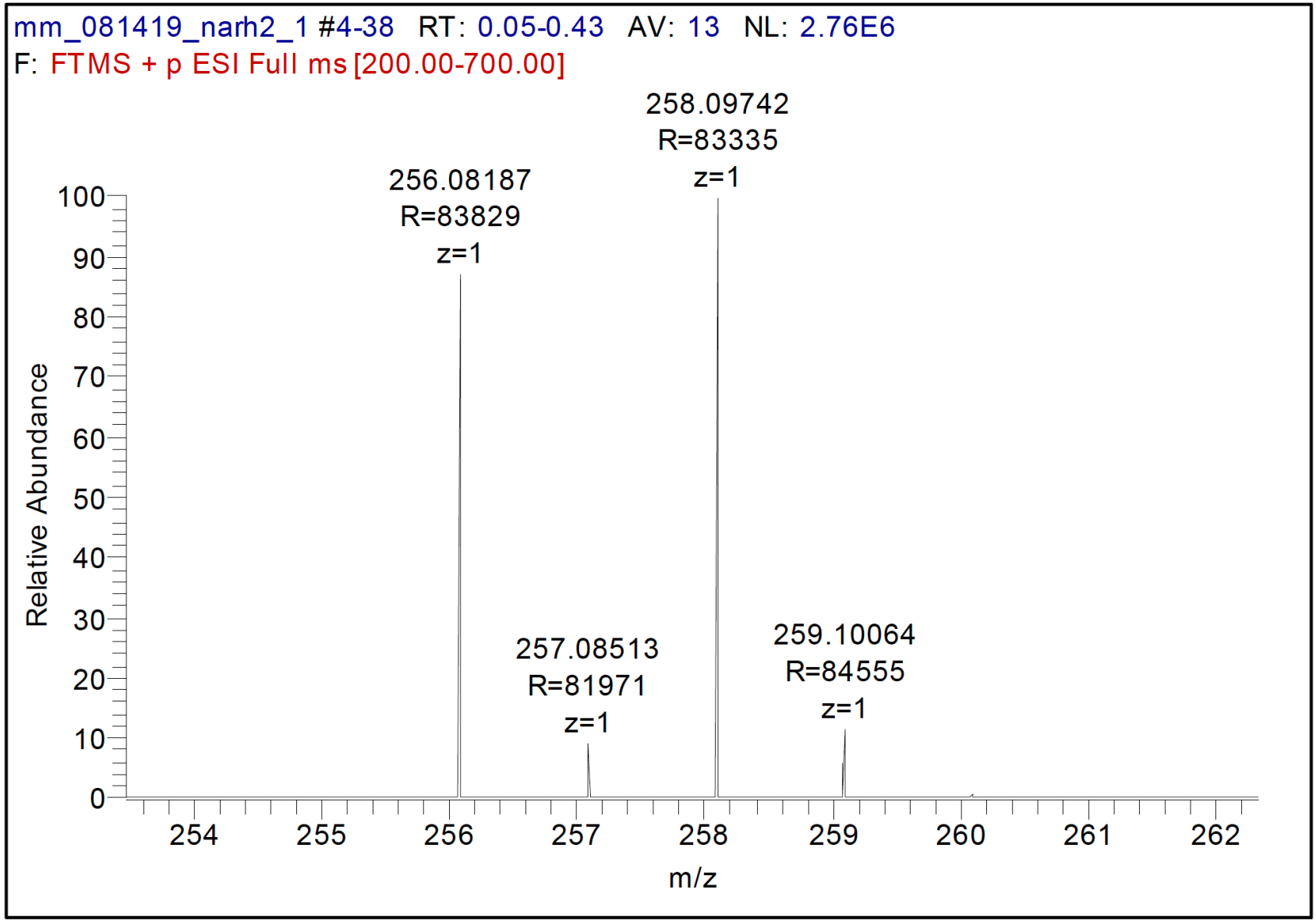



**Figure 57.** HRMS of NARH (**6b**) in 1:1 $H_2O$/ACN.

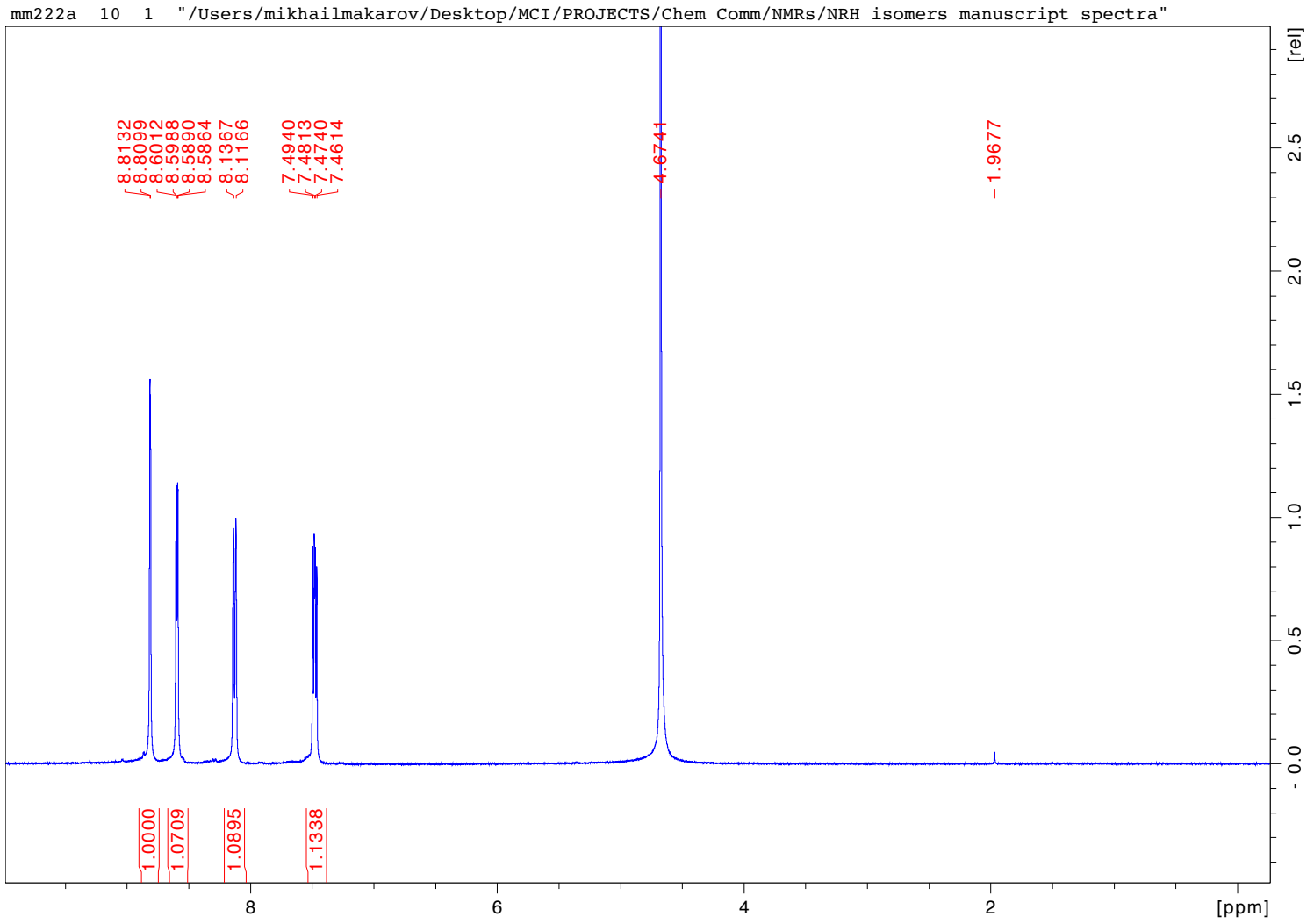



**Figure 58.** $^{1}H$ NMR ($D_2O$) of [$^{18}O$]Nam (**7**).

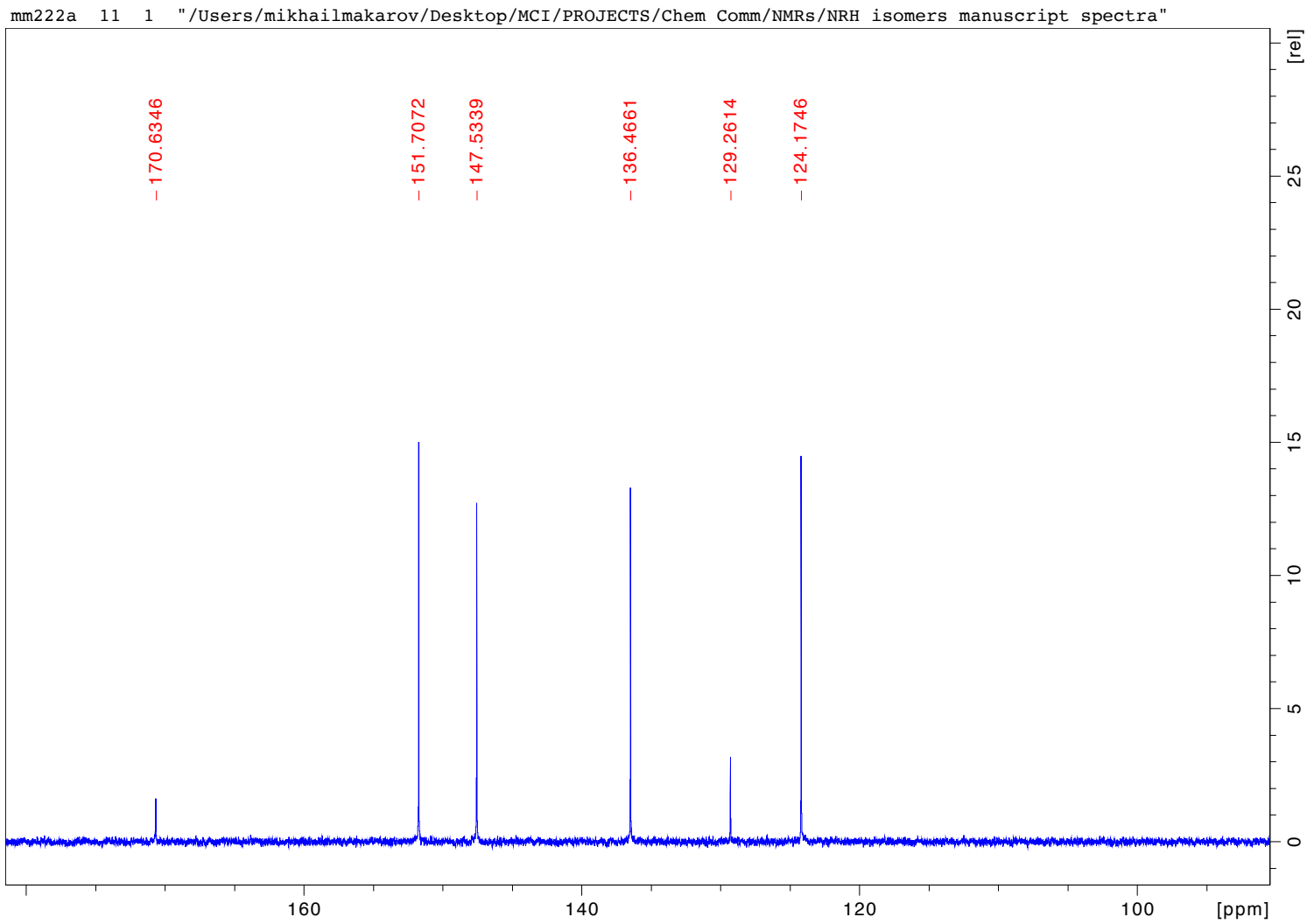



**Figure 59.** $^{13}C$ NMR ($D_2O$) of [$^{18}O$]Nam (**7**).

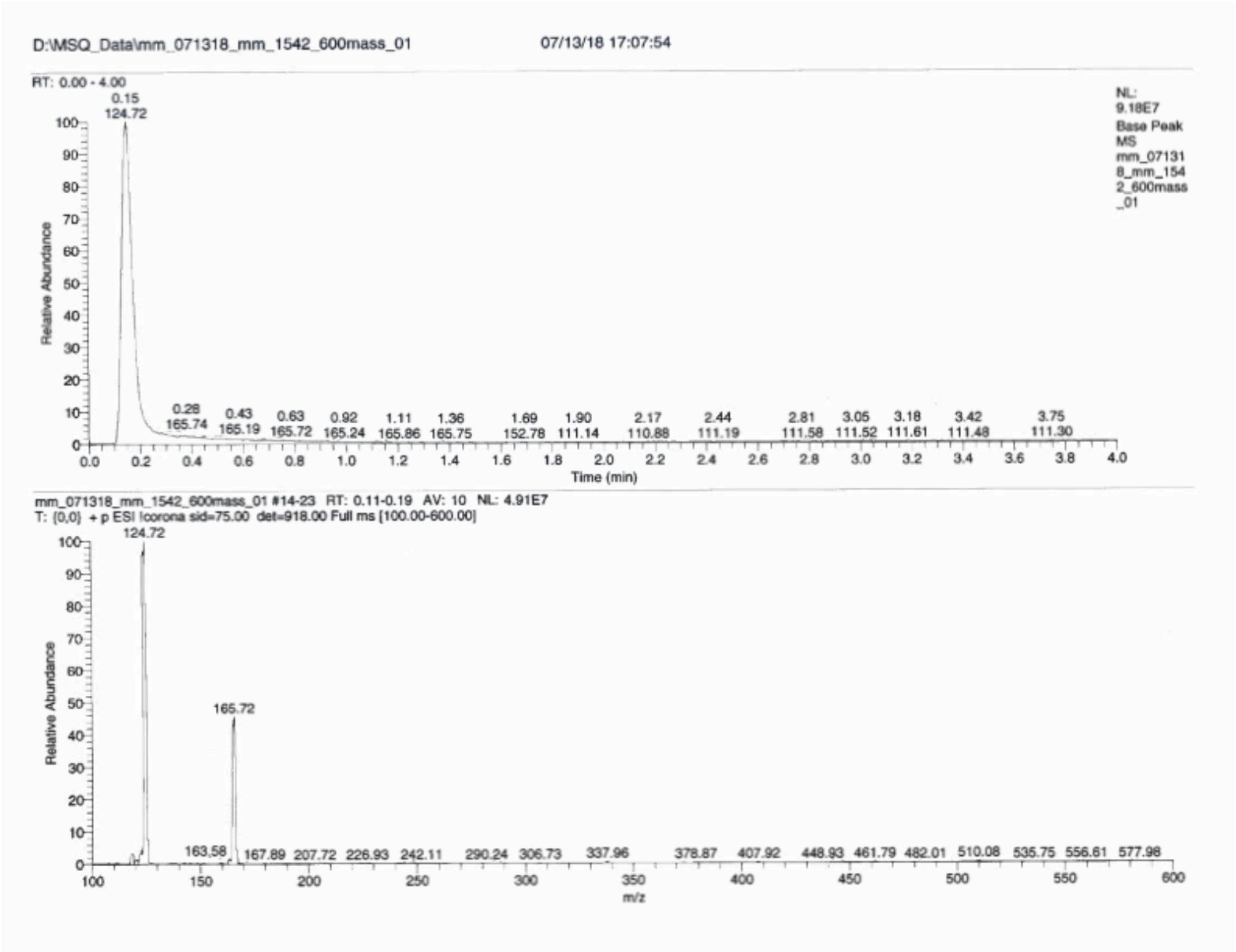



**Figure 60.** MS of [$^{18}$O]Nam (**7**) in 1:1 $H_2O$/ACN.

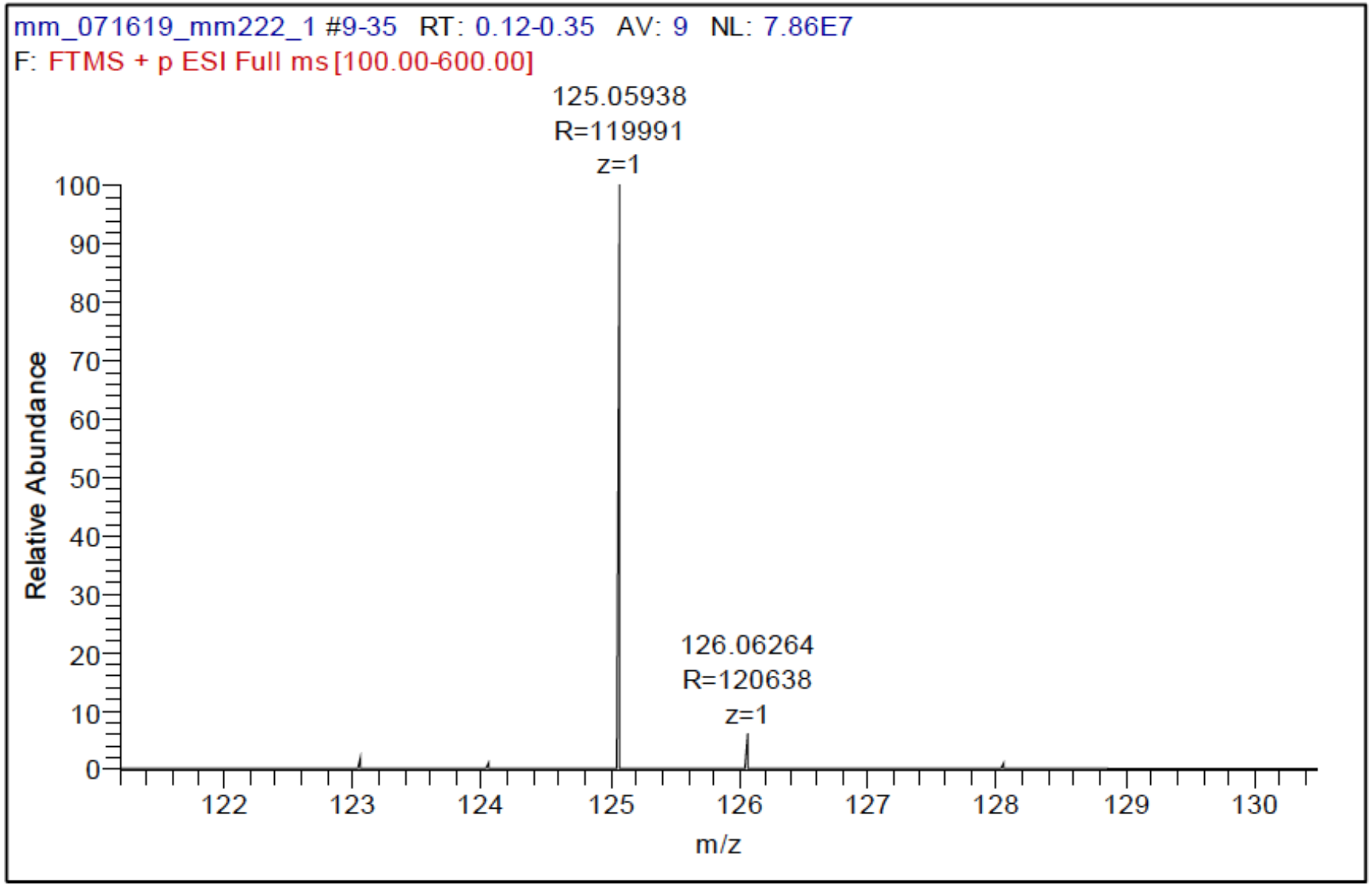



**Figure 61.** HRMS of [$^{18}$O]Nam (**7**) in 1:1 $H_2O$/ACN.

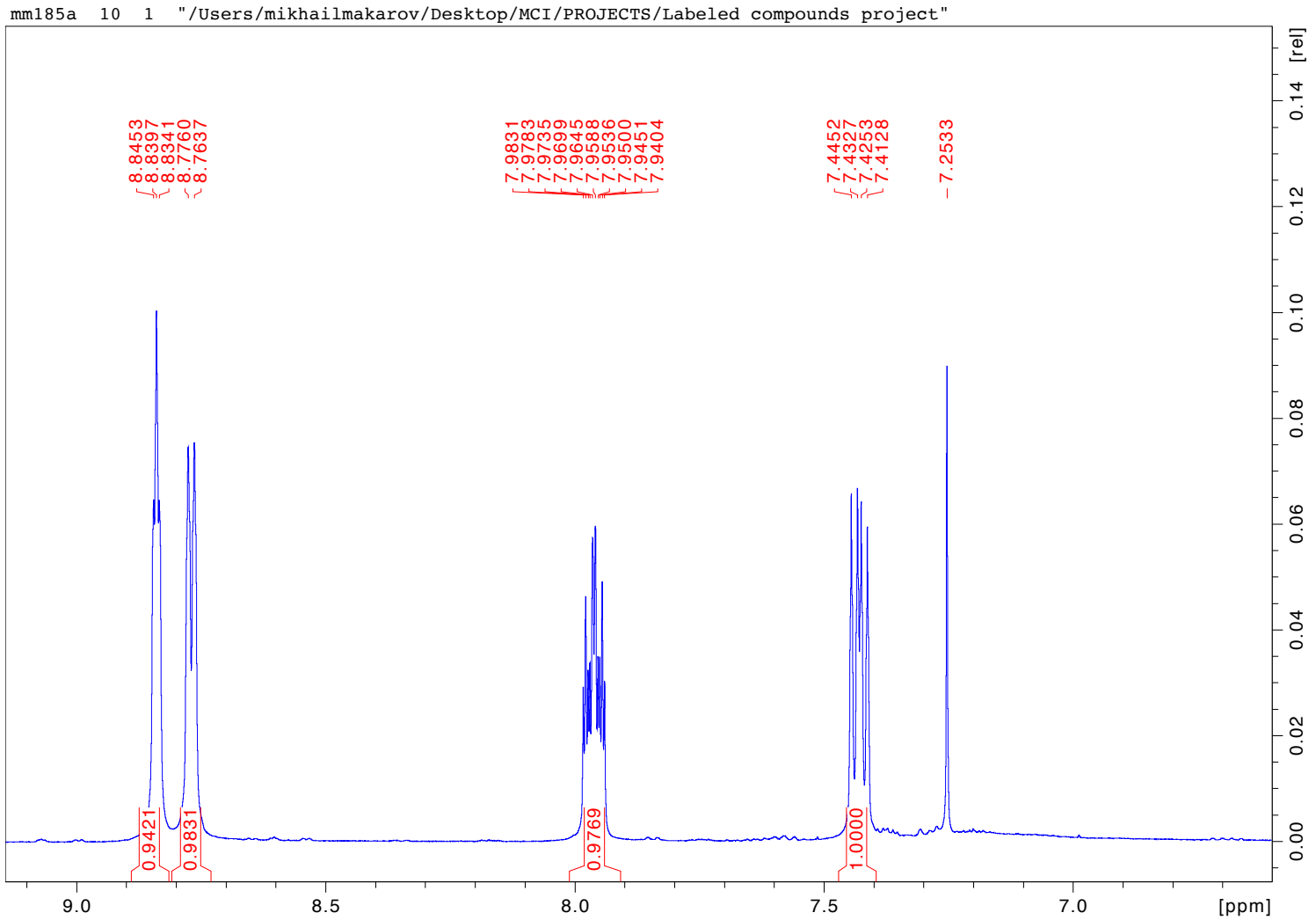



**Figure 62.** $^{1}$H NMR ($CDCl_3$) of [*$^{13}$C-nitrile*]Nicotinonitrile (**14**).

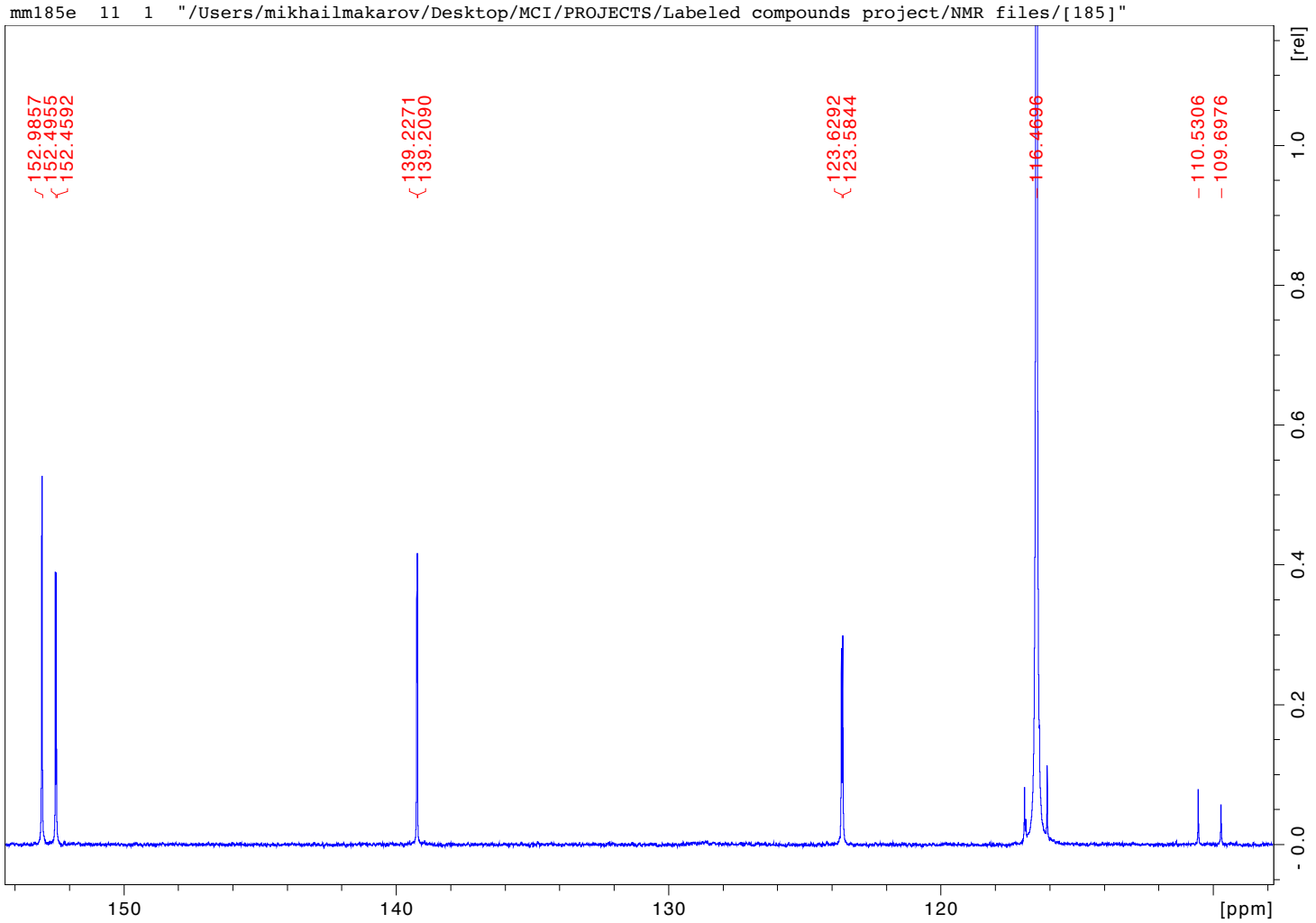



**Figure 63.** $^{13}C$ NMR ($CDCl_3$) of [*$^{13}C$-nitrile*]Nicotinonitrile (**14**).

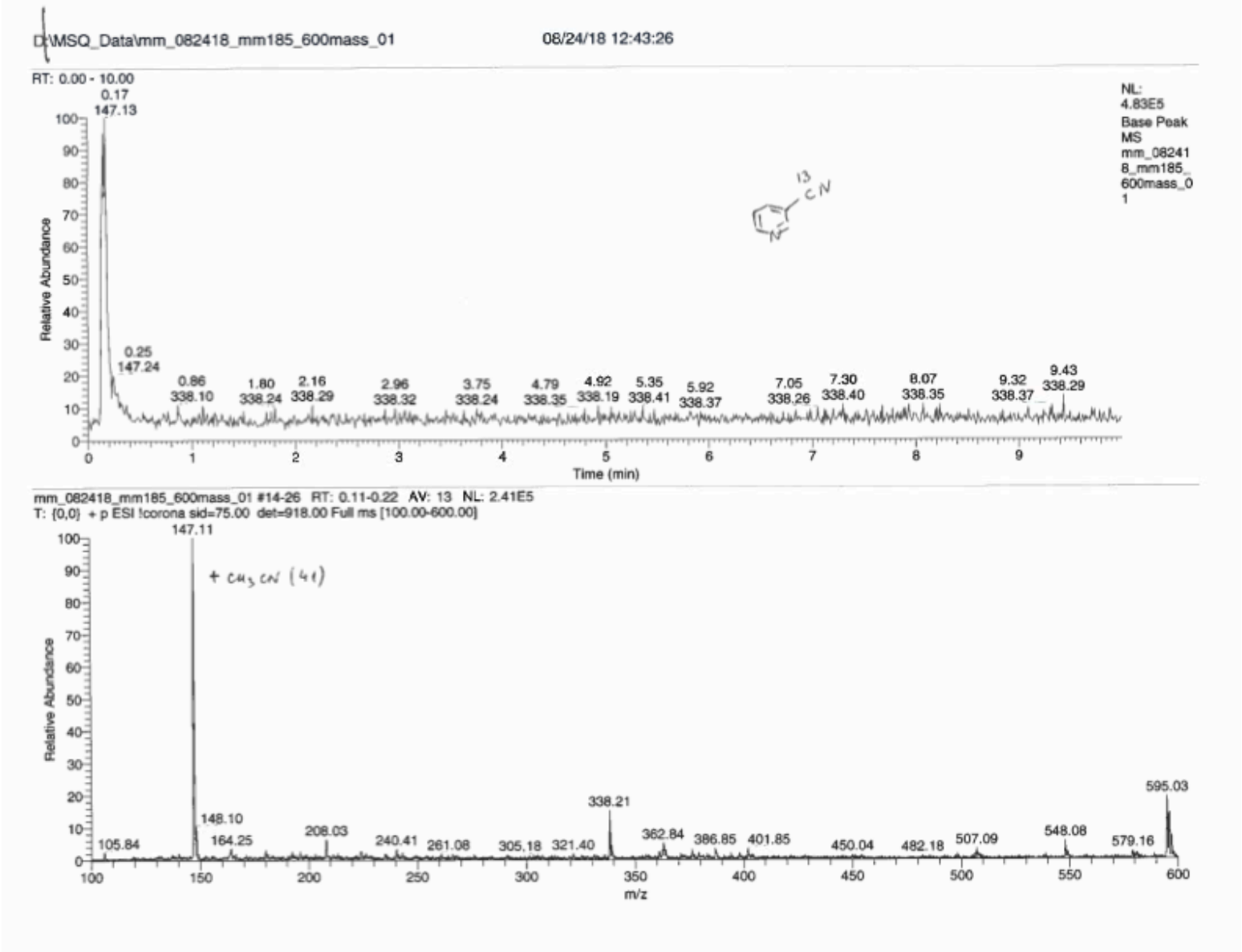



**Figure 64.** MS of [*$^{13}$C-nitrile*]Nicotinonitrile (**14**) in 1:1 $H_2O$/ACN.

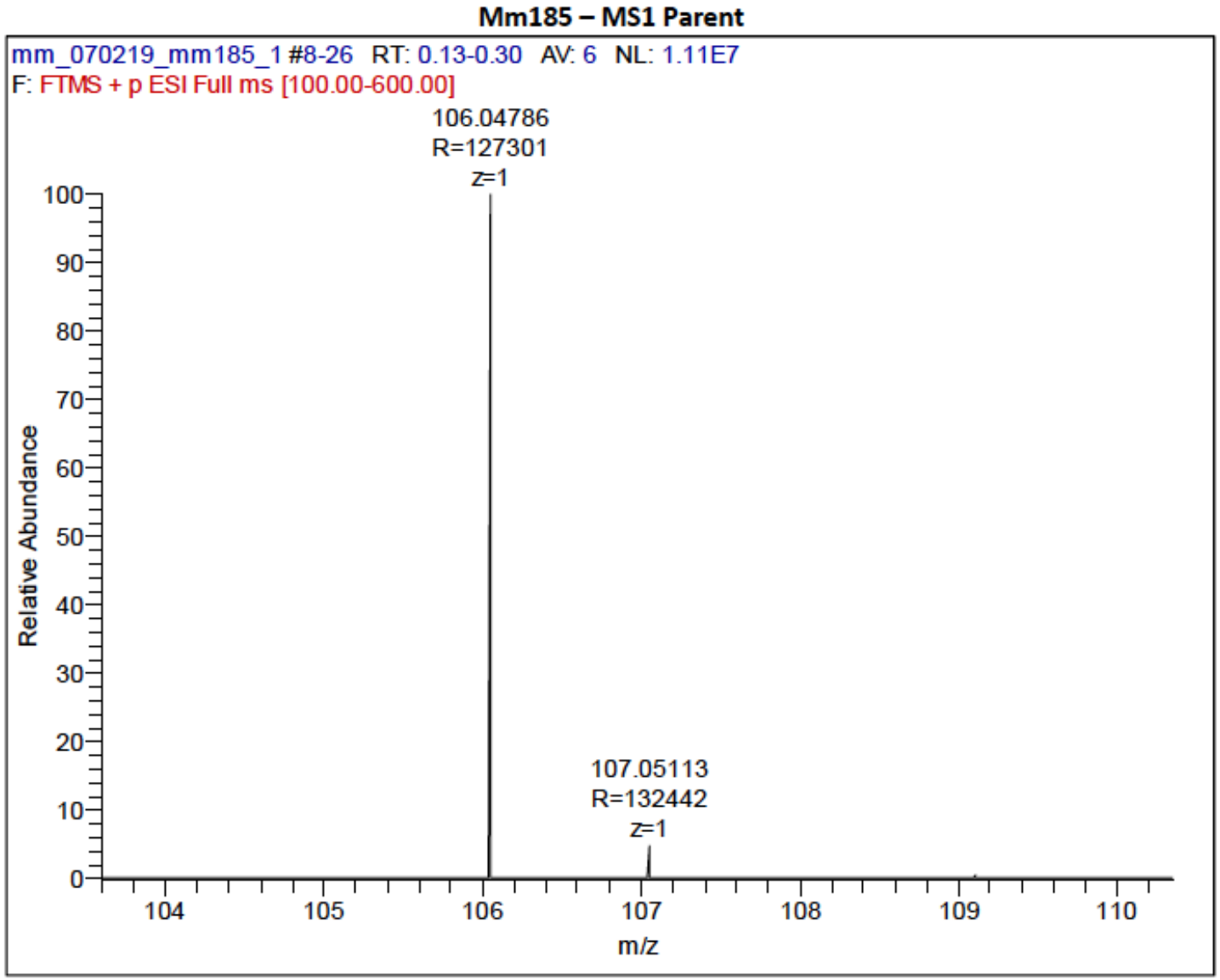



**Figure 65.** HRMS of [$^{13}$*C-nitrile*]Nicotinonitrile (**14**) in 1:1 $H_2O$/ACN.

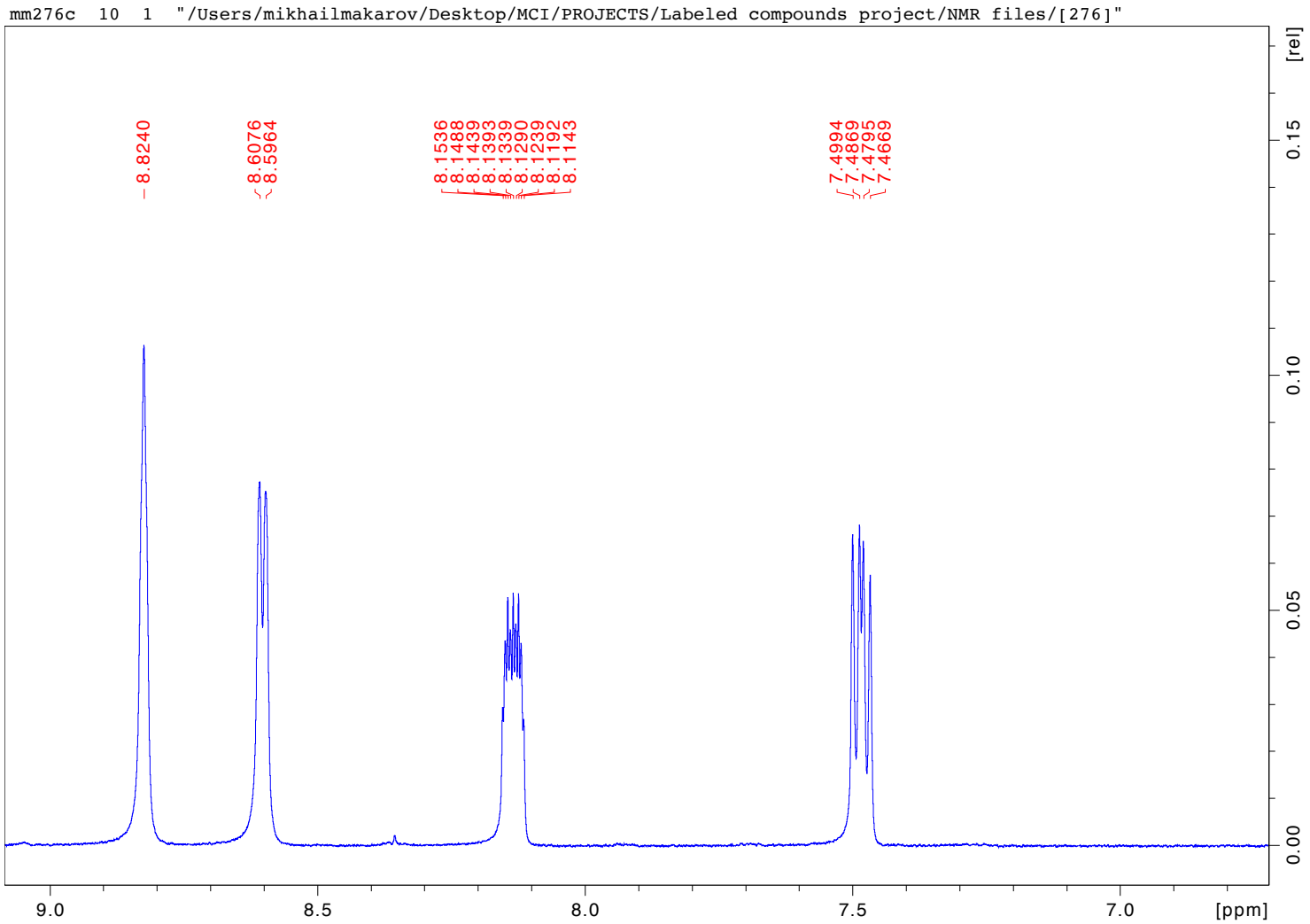



**Figure 66.** $^{1}$H NMR ($D_2O$) of [*$^{18}O$,$^{13}C$-carbonyl*]Nicotinamide (**15**).

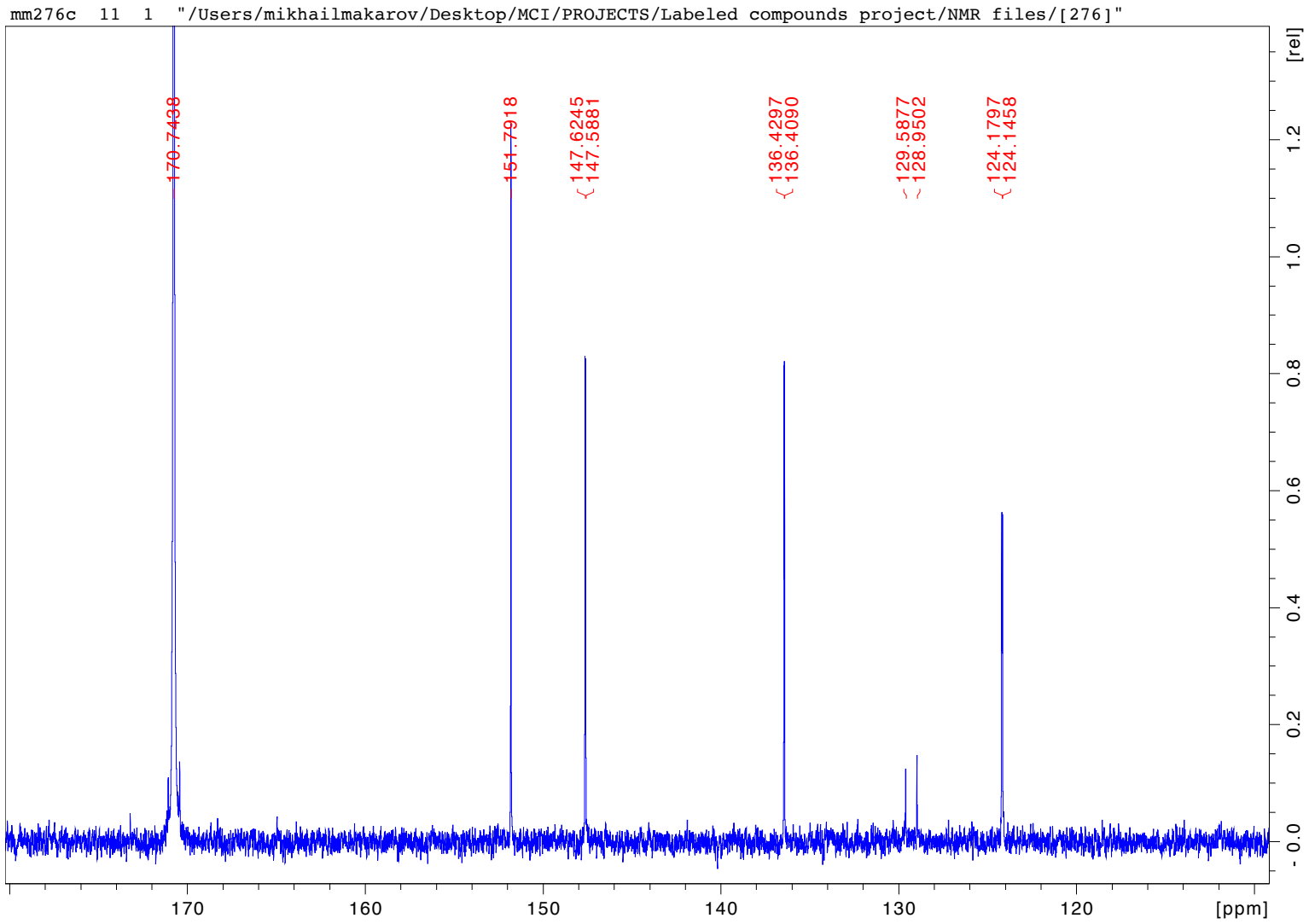



**Figure 67.** $^{13}C$ NMR ($D_2O$) of [*$^{18}O$,$^{13}C$-carbonyl*]Nicotinamide (**15**).

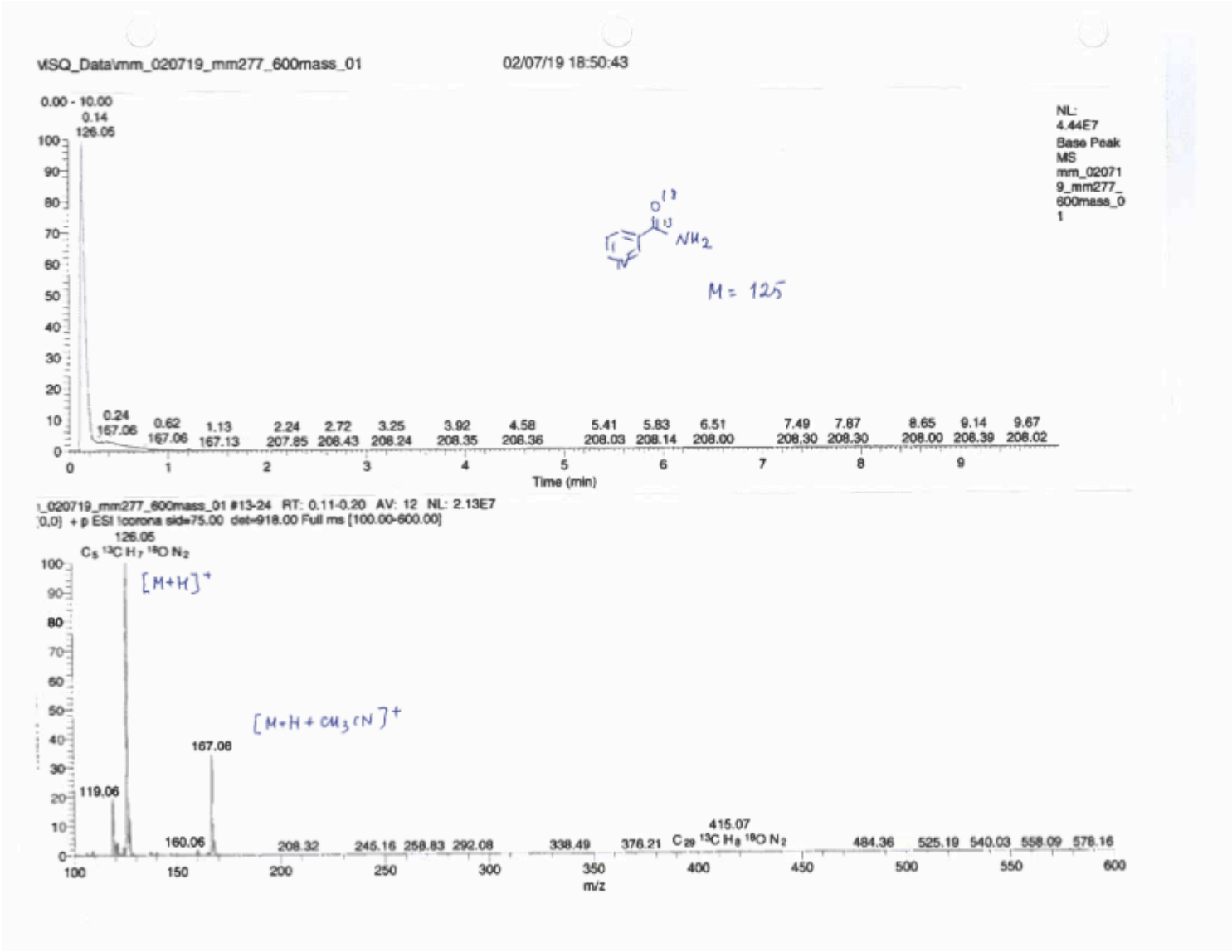



**Figure 68.** MS of [*$^{18}O$,$^{13}C$-carbonyl*]Nicotinamide (**15**) in 1:1 $H_2O$/ACN.

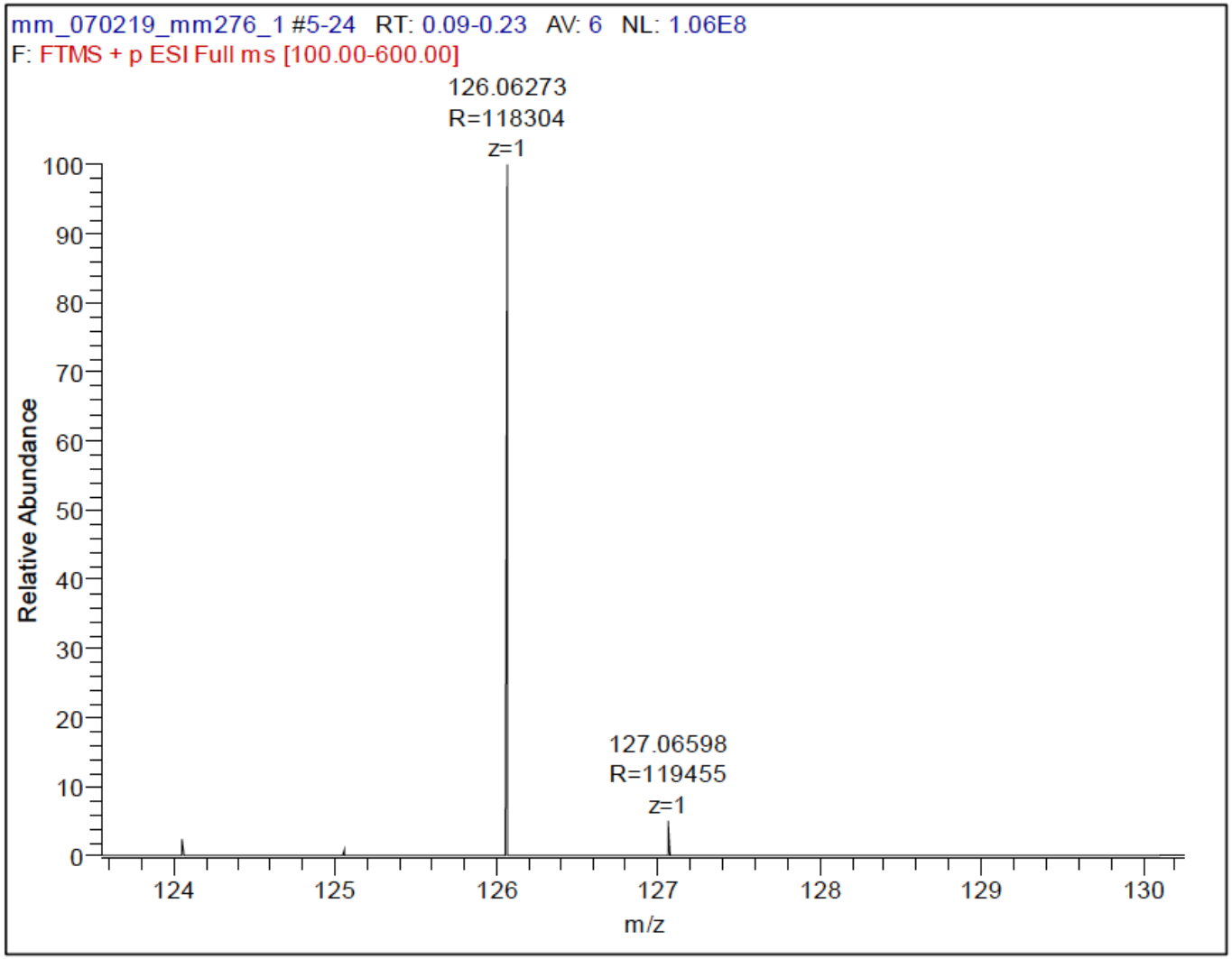



**Figure 69.** HRMS of [$^{18}O,^{13}C$-*carbonyl*]Nicotinamide (**15**) in 1:1 $H_2O$/ACN.

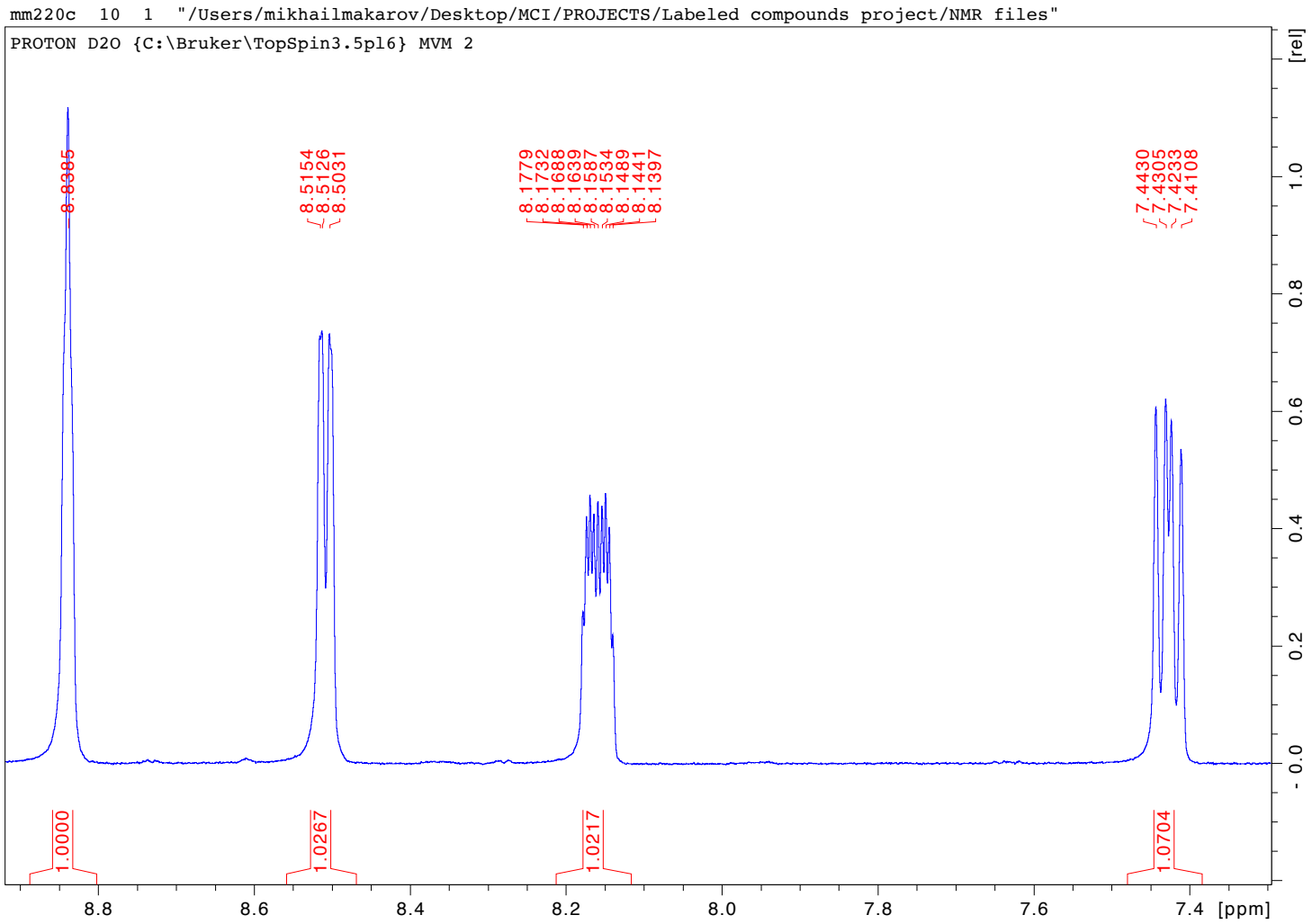



**Figure 70.** $^{1}$H NMR ($D_2O$) of [*$^{13}$C-carbonyl*]Nicotinic acid, sodium salt (**16**).

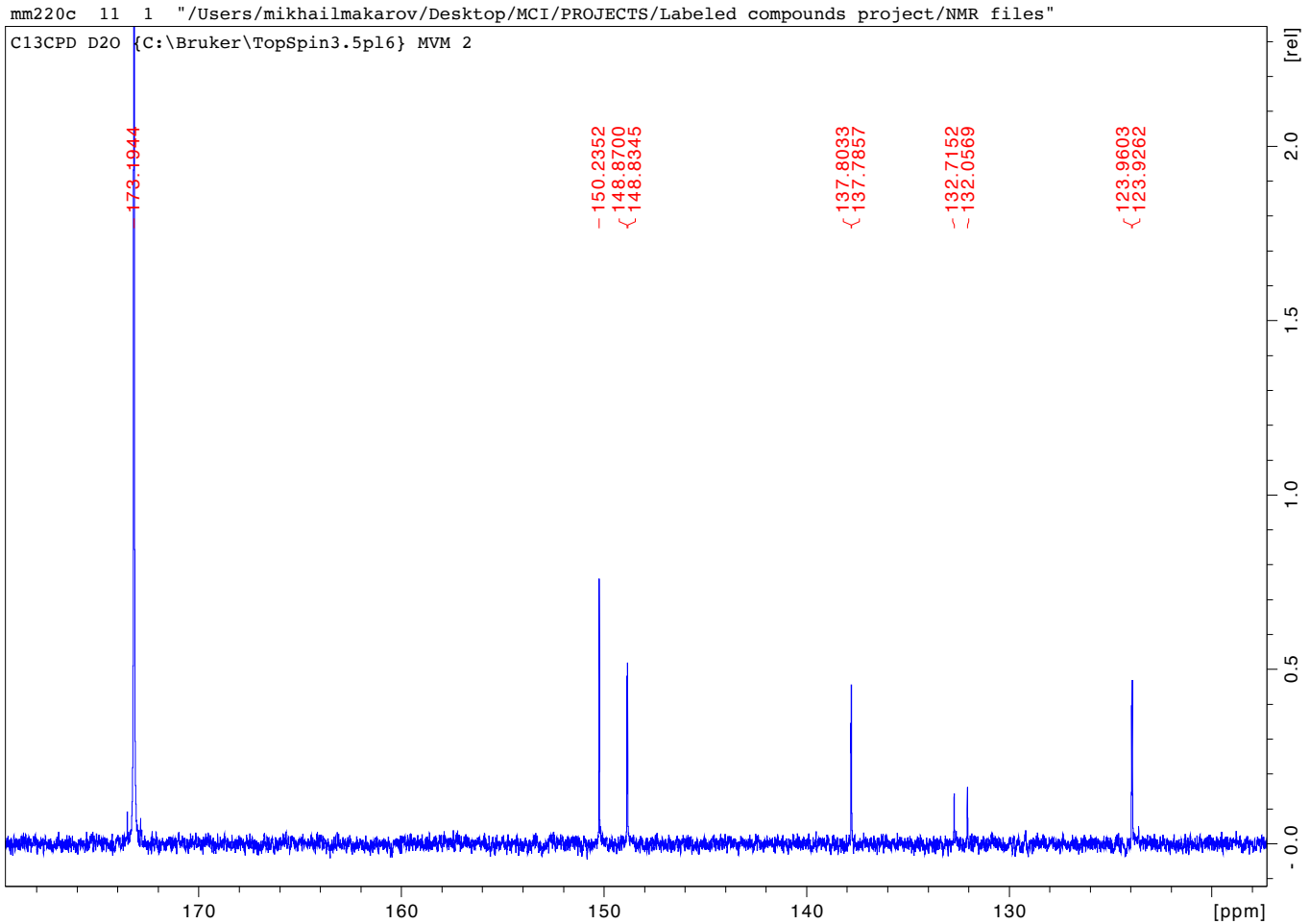



**Figure 71.** $^{13}C$ NMR ($D_2O$) of [*$^{13}C$-carbonyl*]Nicotinic acid, sodium salt (**16**).

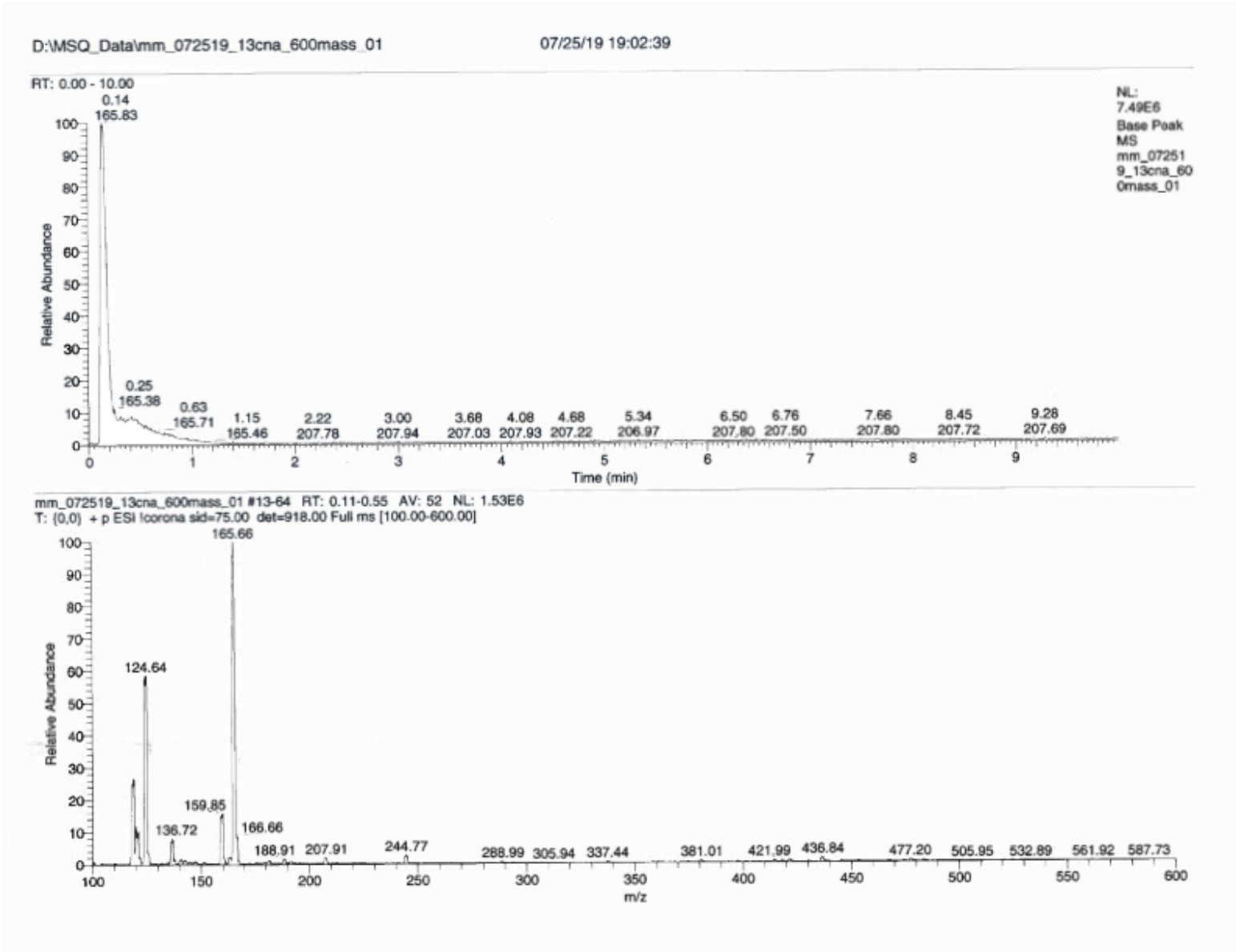



**Figure 72.** MS of [$^{13}$*C-carbonyl*]Nicotinic acid, sodium salt (**16**), in 1:1 $H_2O$/ACN.

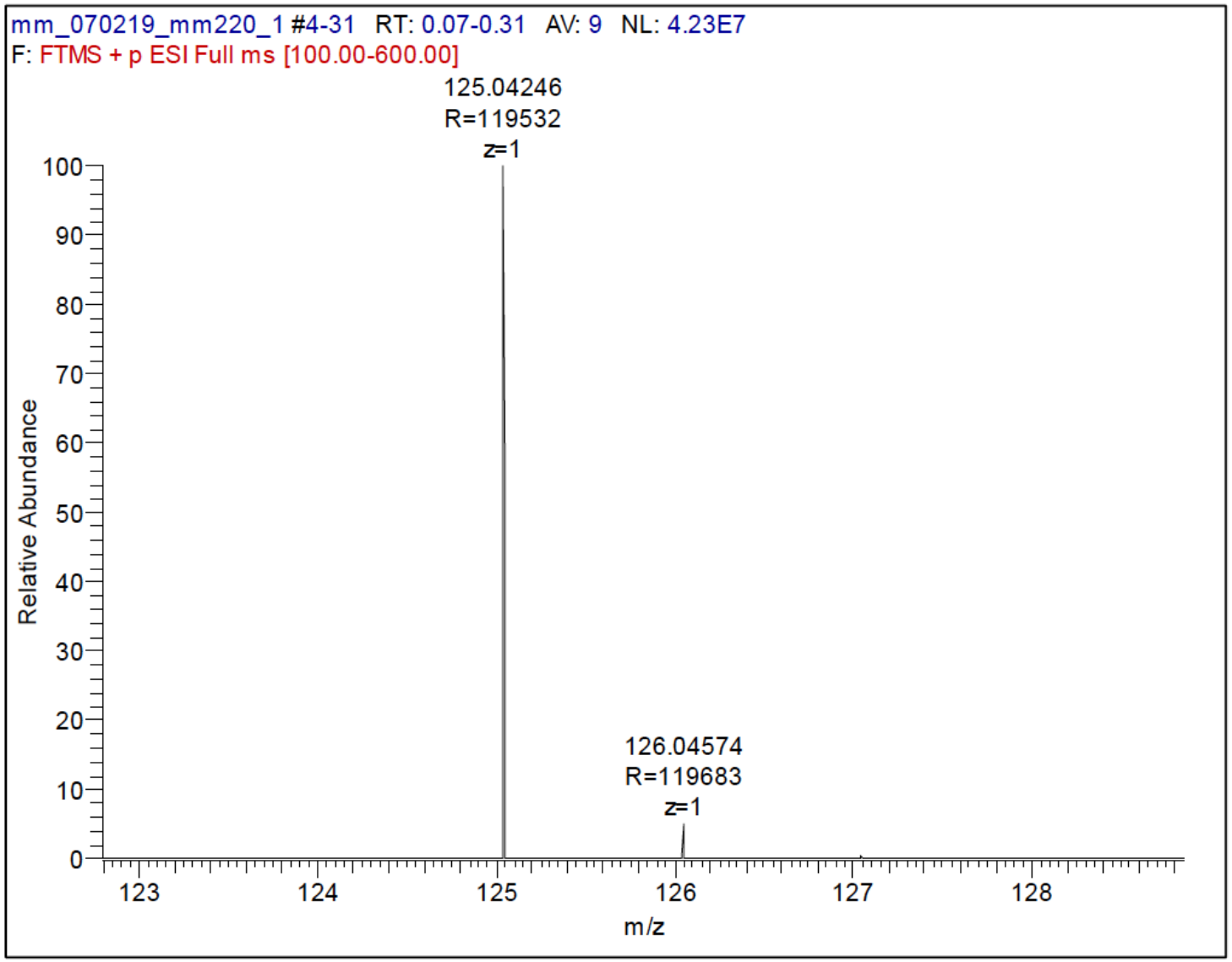



**Figure 73.** HRMS of [$^{13}$*C-carbonyl*]Nicotinic acid, sodium salt (**16**), in 1:1 $H_2O$/ACN.

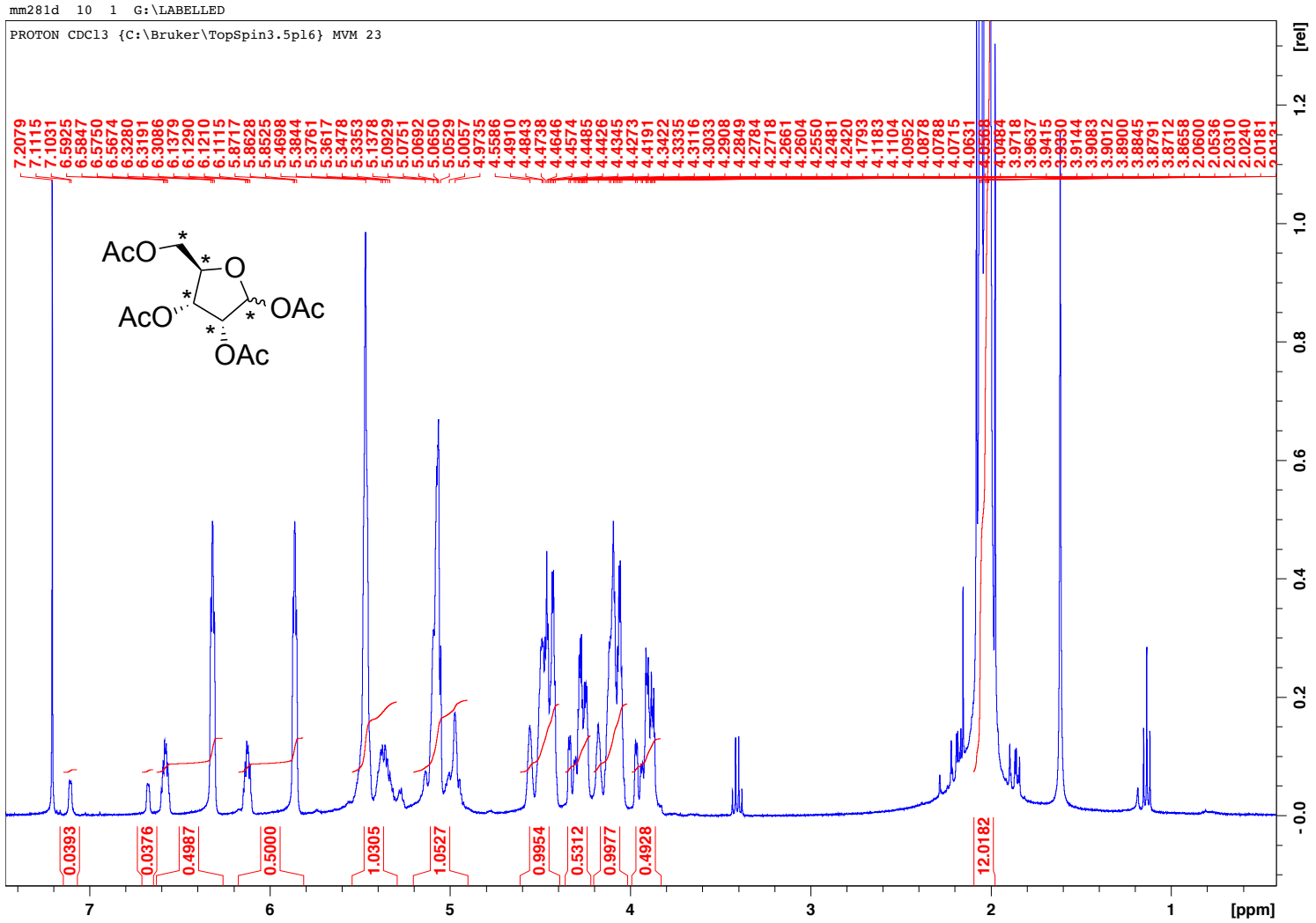



**Figure 74.** $^{1}$H NMR ($CDCl_3$) of 1,2,3,5-Tetra-*O*-acetyl-α/β-D-[$^{13}C_5$]ribofuranose ([$^{13}C_5$]RTA, **9**) general view.

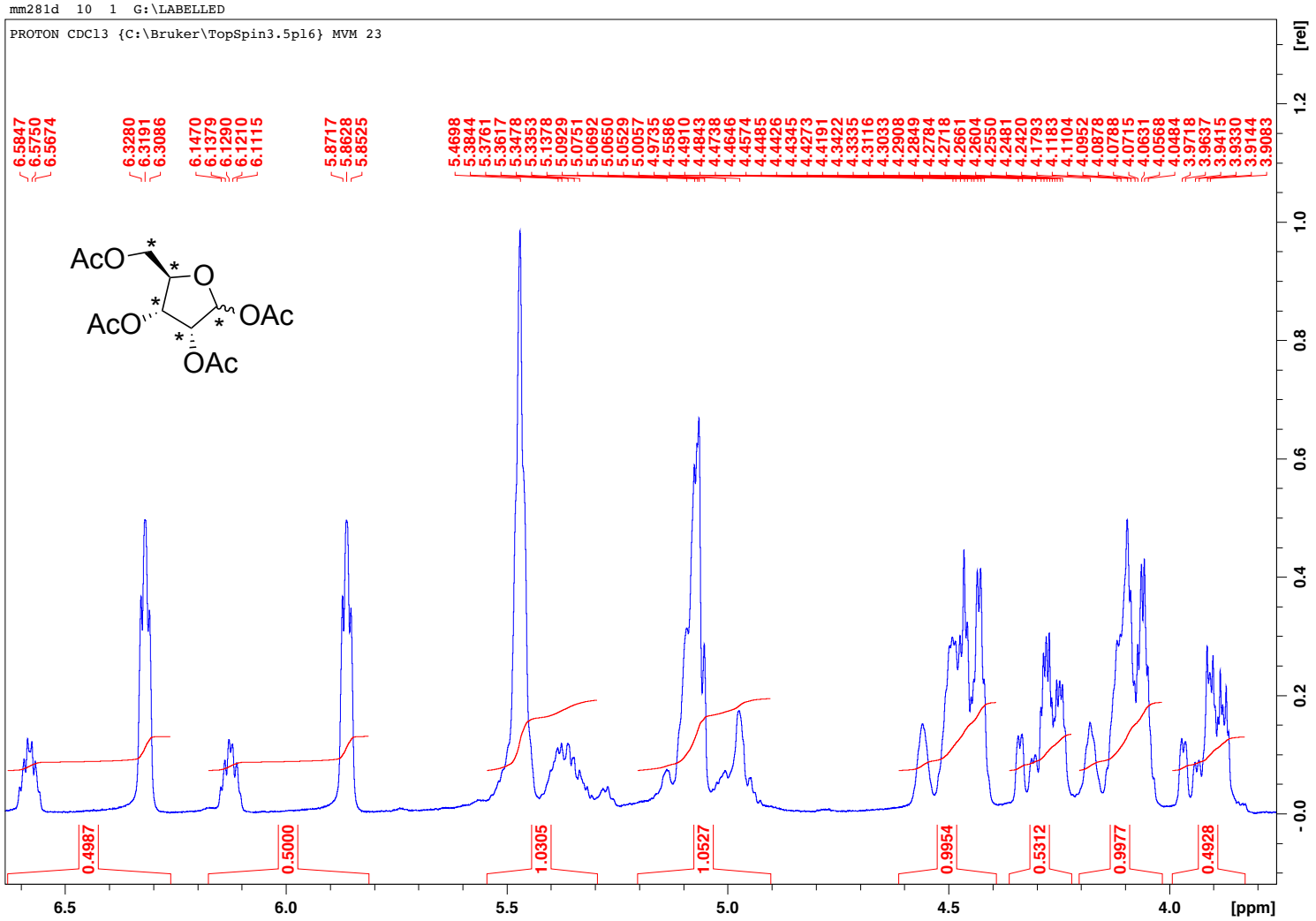



**Figure 75.** $^{1}$H NMR ($CDCl_3$) of 1,2,3,5-Tetra-*O*-acetyl-α/β-D-[$^{13}C_5$]ribofuranose ([$^{13}C_5$]RTA, **9**), zoomed from ca. 3.8 to 6.6 ppm.

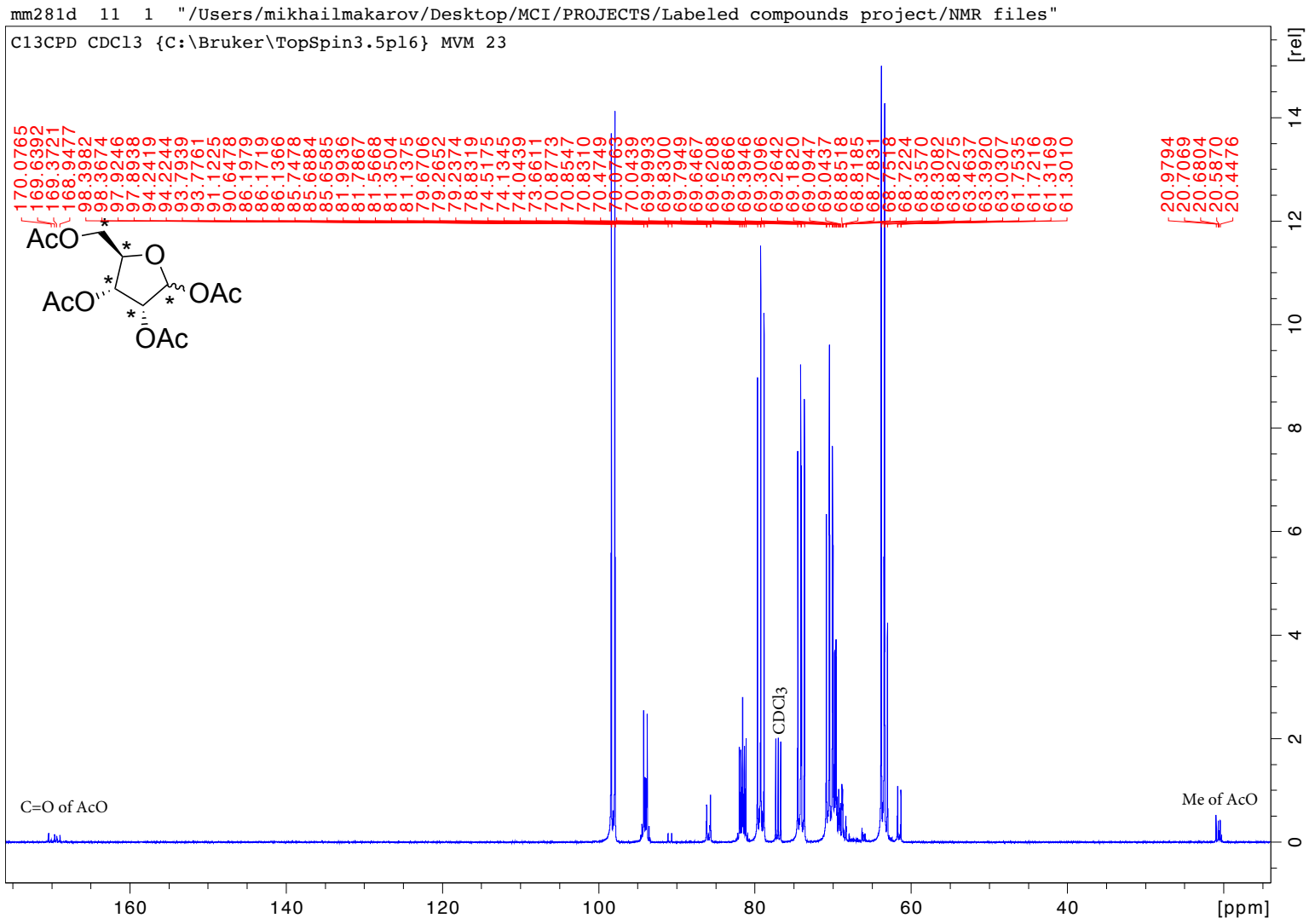



**Figure 76.** $^{13}C$ NMR ($CDCl_3$) of 1,2,3,5-Tetra-*O*-acetyl-α/β-D-[$^{13}C_5$]ribofuranose ([$^{13}C_5$]RTA, **9**), general view.

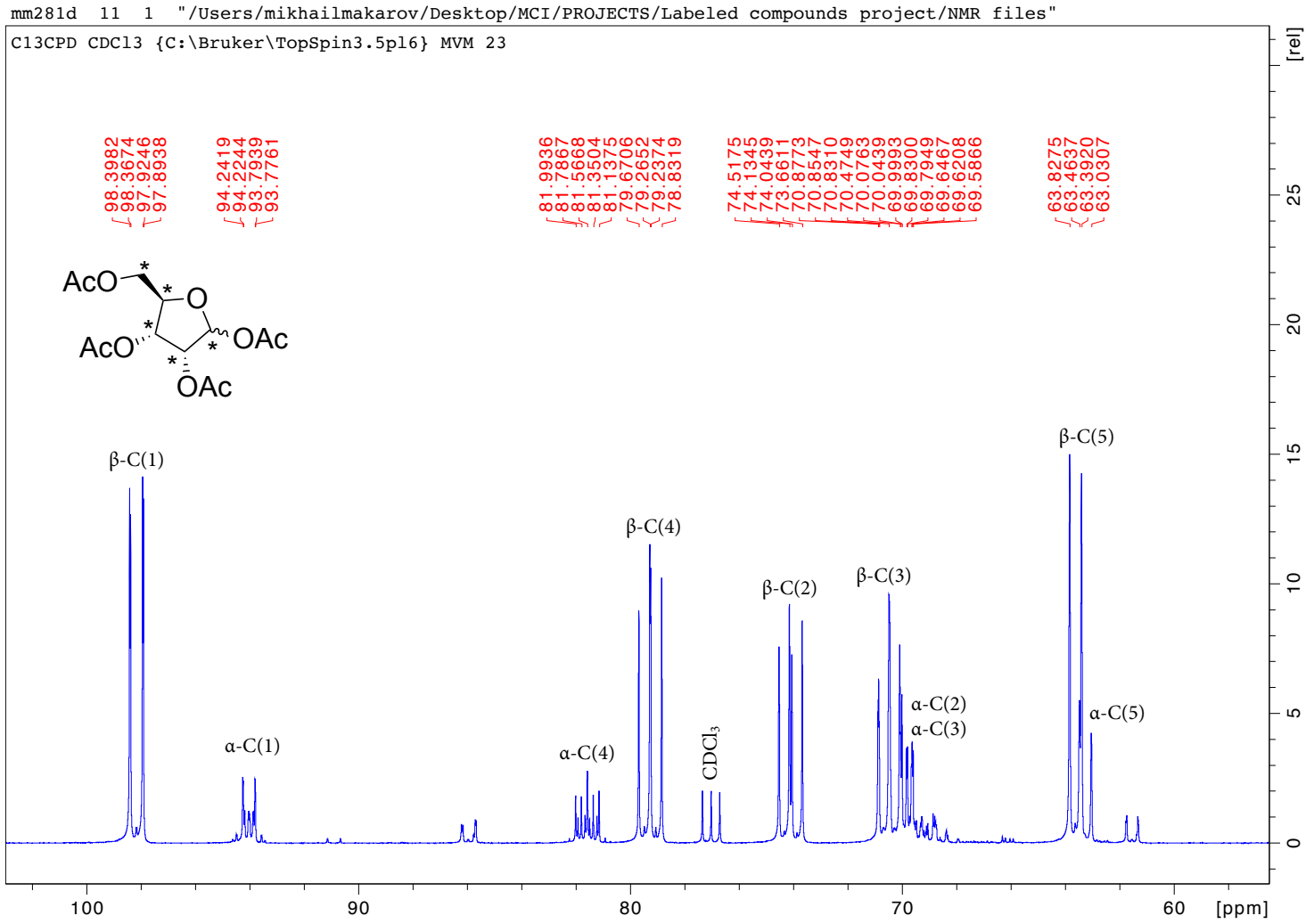



**Figure 77.** $^{13}$H NMR ($CDCl_3$) of 1,2,3,5-Tetra-*O*-acetyl-α/β-D-[$^{13}C_5$]ribofuranose ([$^{13}C_5$]RTA, **9**), zoomed from 58 to 102 ppm.

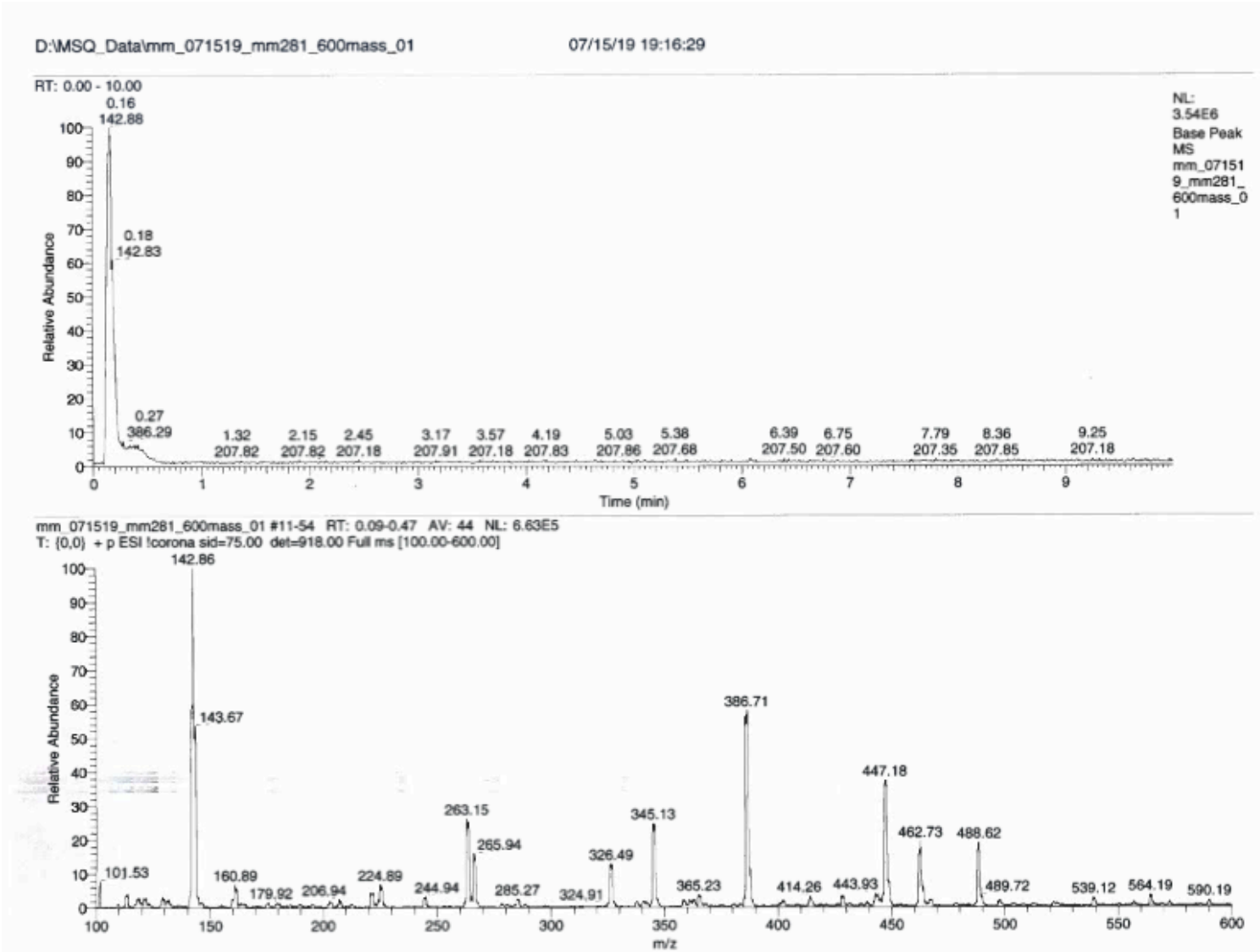



**Figure 78.** MS of [$^{13}C_5$]Ribose tetraacetate ([$^{13}C_5$]RTA, **9**) in 1:1 $H_2O$/ACN, *m/z*: 263.15 ([M–OAc]$^+$), 345.13 ([M+Na]$^+$), 386.71 ([M+Na+$CH_3CN$]$^+$).

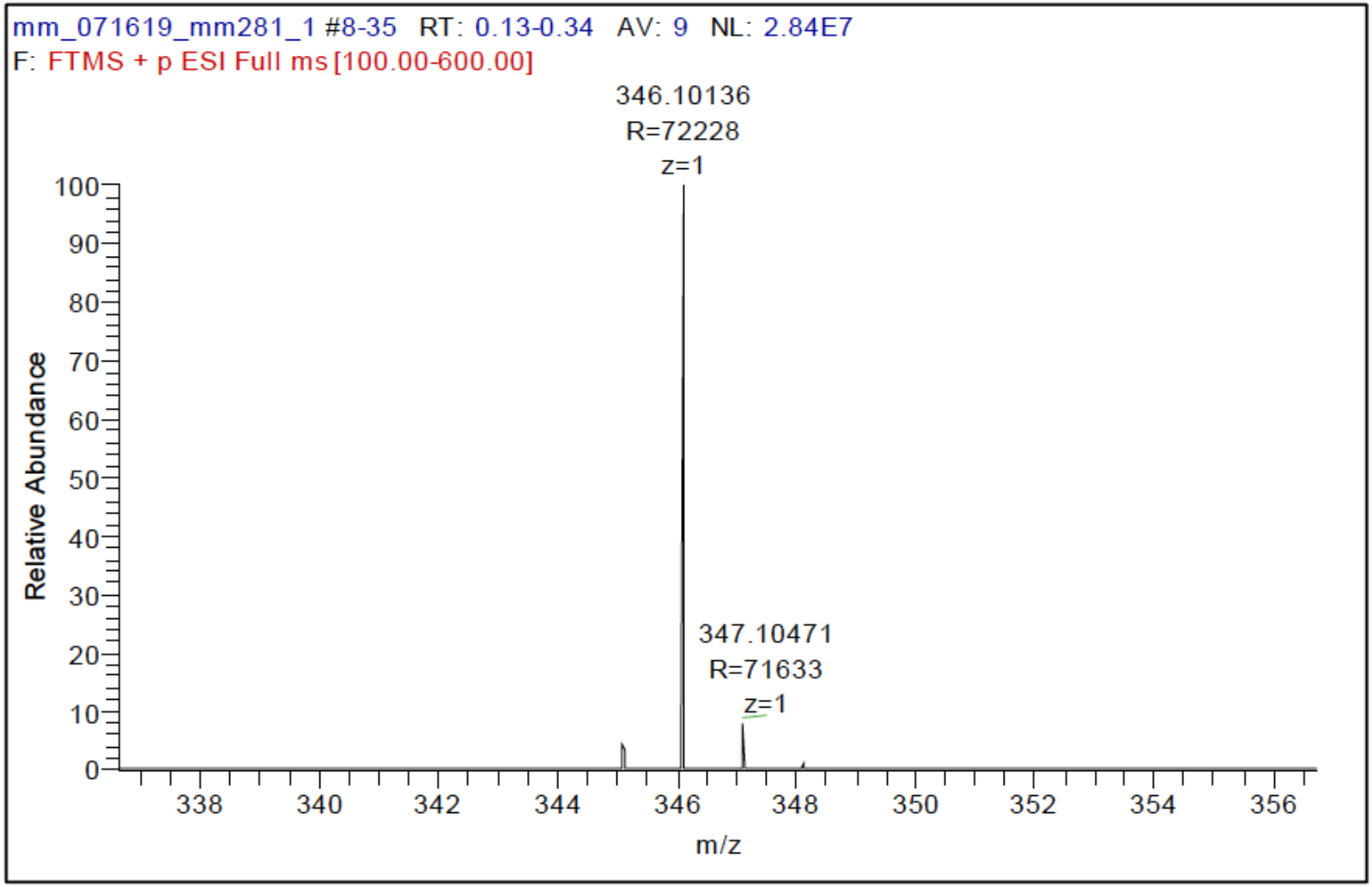



**Figure 79.** HRMS of [$^{13}C_5$]Ribose tetraacetate ([$^{13}C_5$]RTA, **9**) in 1:1 $H_2O$/ACN: $[M+Na]^+$ peak (m/z = 346.10136).

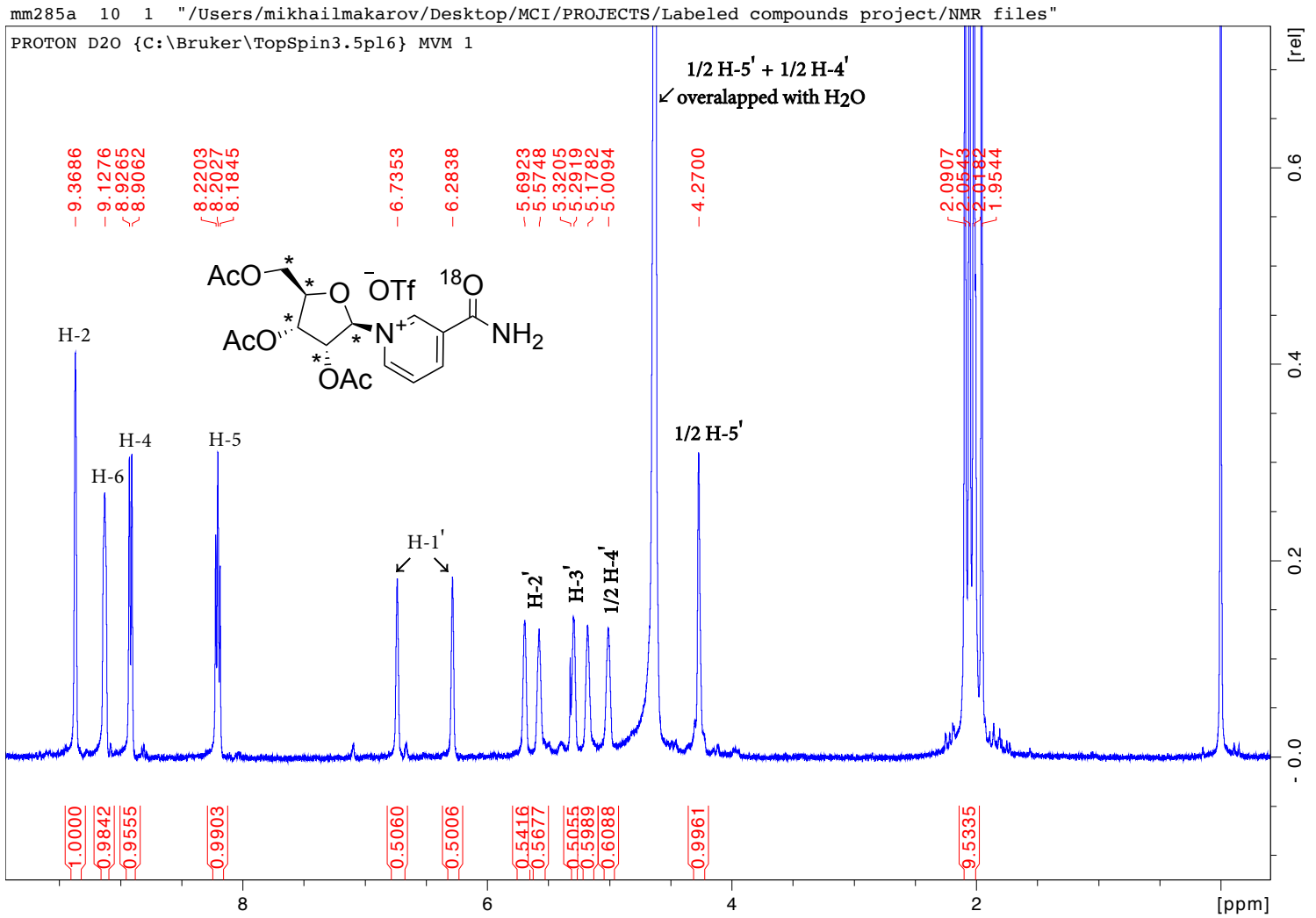



**Figure 80.** $^{1}H$ NMR ($D_2O$) of [$^{13}C_5$,$^{18}O$]NR TA OTf (m+7) (**10**).

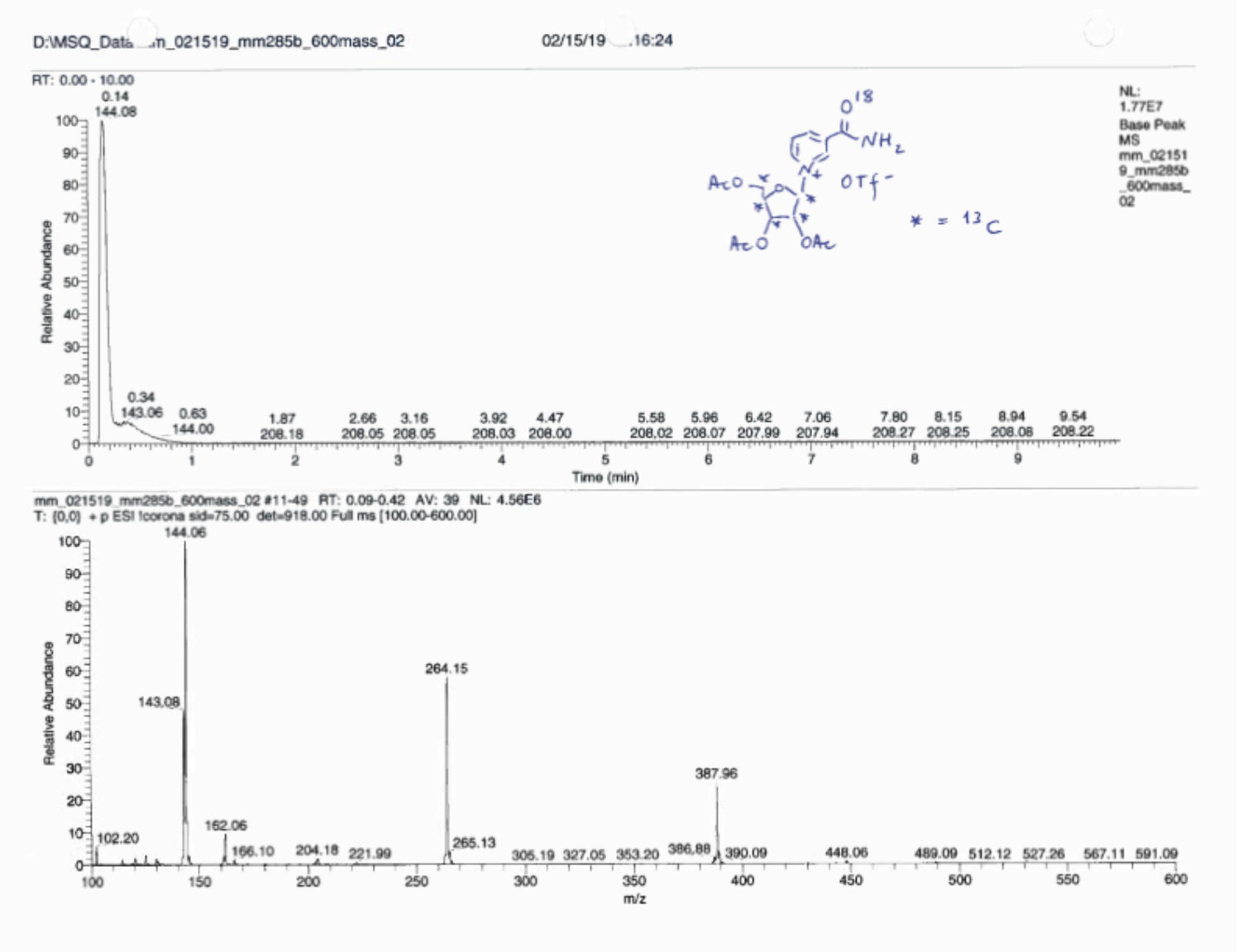



**Figure 81.** MS of NR TA OTf (m+7) (**10**) in 1:1 $H_2O$/ACN.

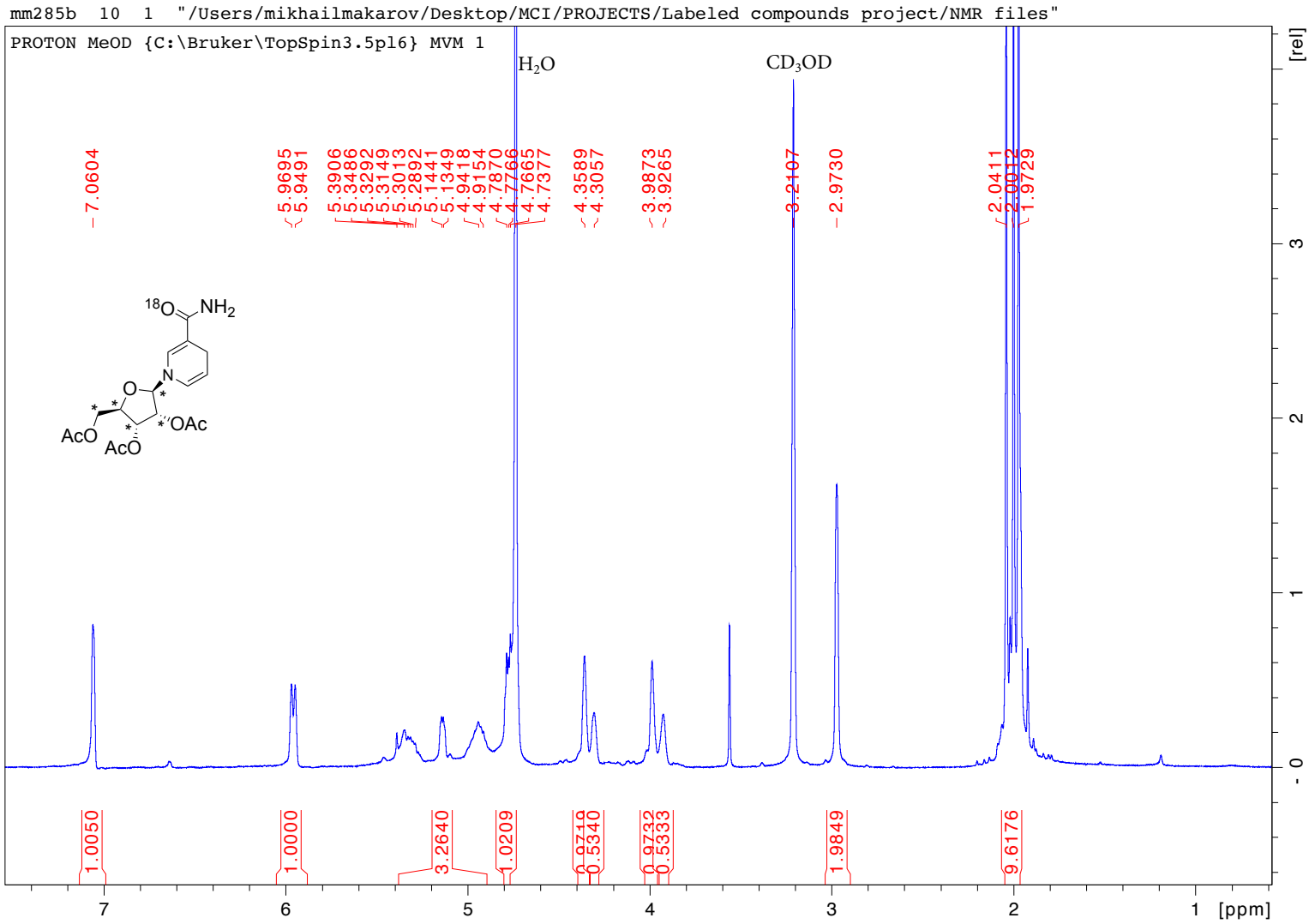



**Figure 82.** $^{1}H$ NMR ($CD_3OD$) of [$^{13}C_5$,$^{18}O$]NRH TA (m+7) (**12**).

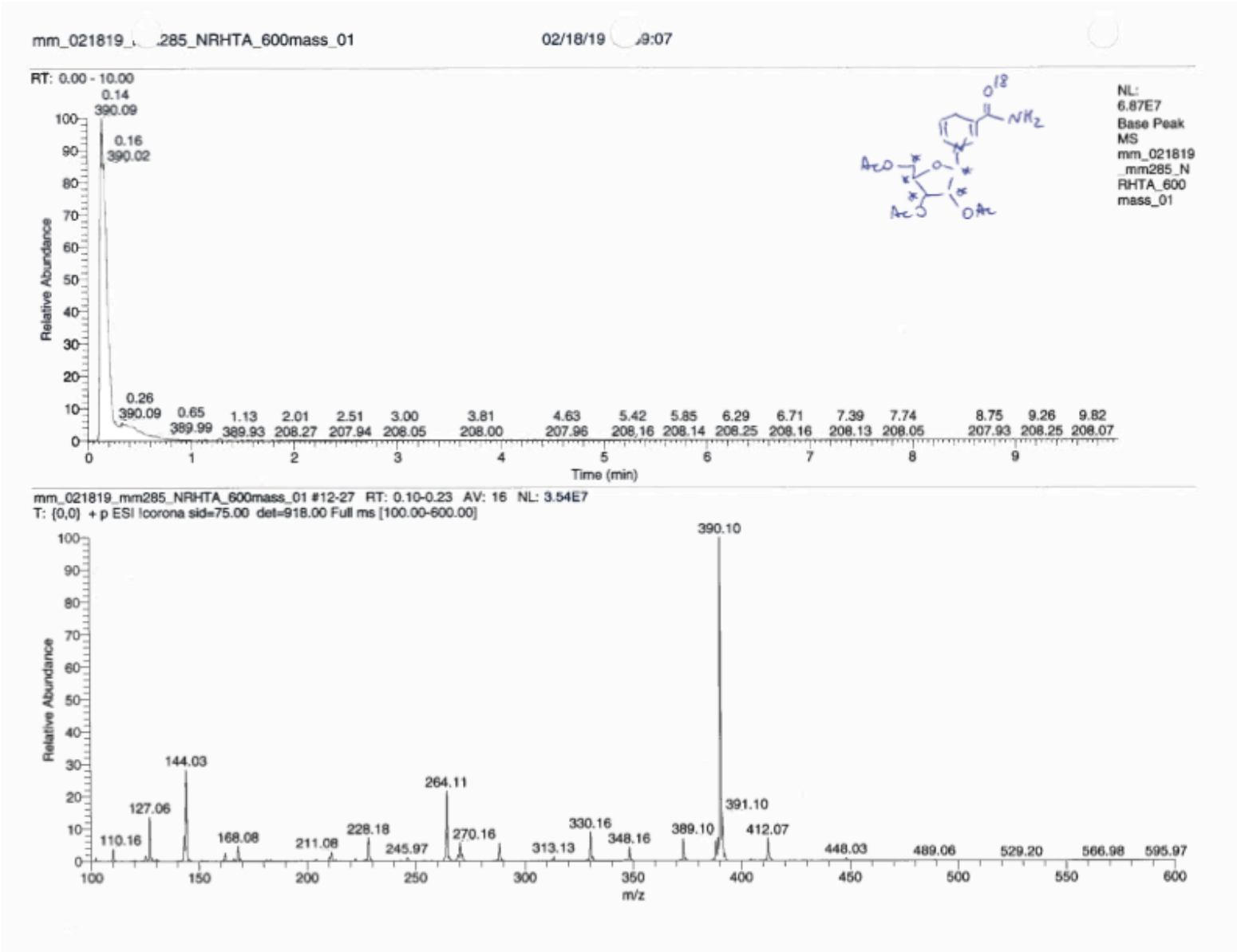



**Figure 83.** MS of [$^{13}C_5$,$^{18}O$]NRH TA (m+7) (**12**) in 1:1 $H_2O$/ACN.

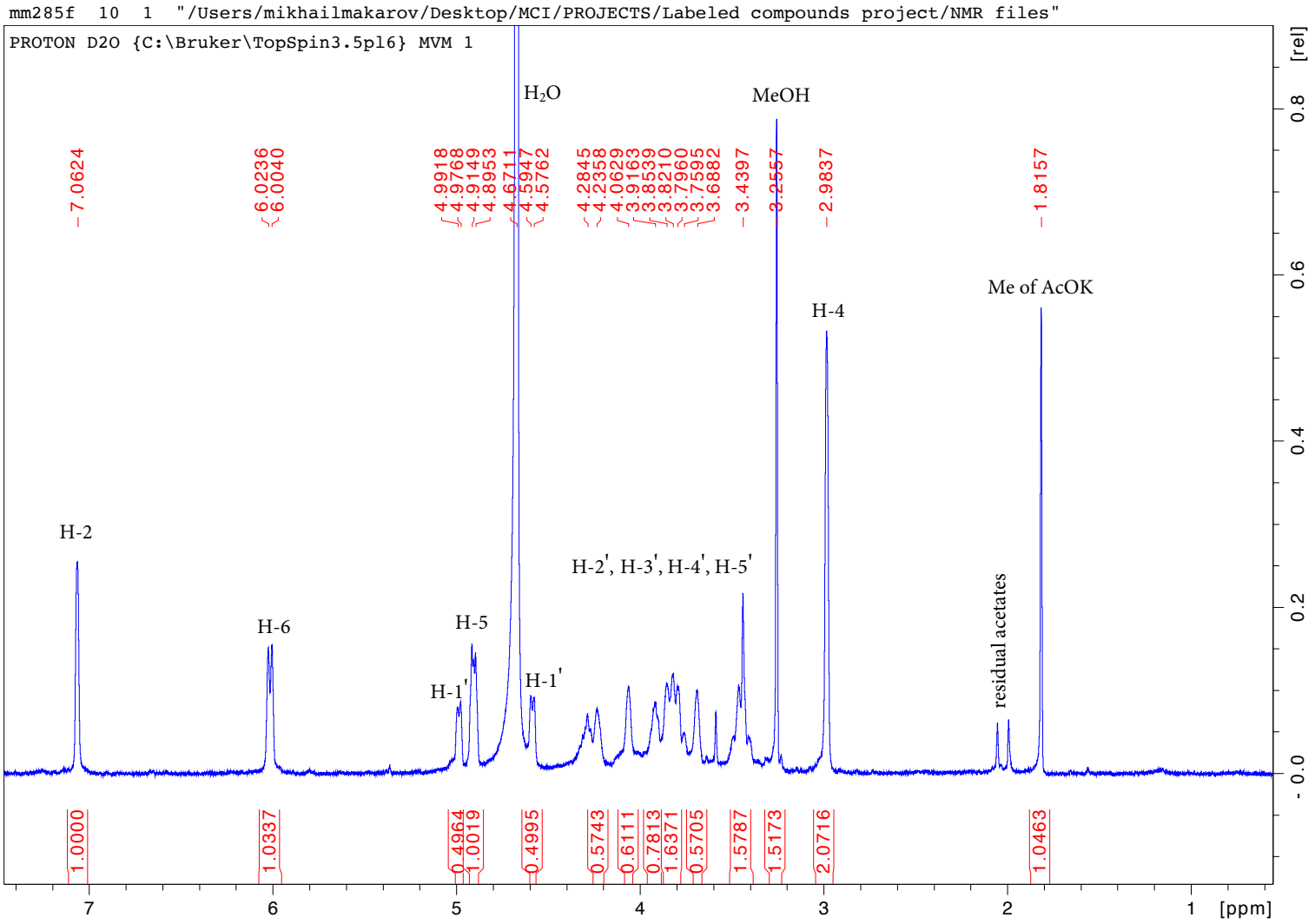



**Figure 84.** $^{1}H$ NMR ($D_2O$) of [$^{13}C_5$,$^{18}O$]NRH (m+7) (**13**).

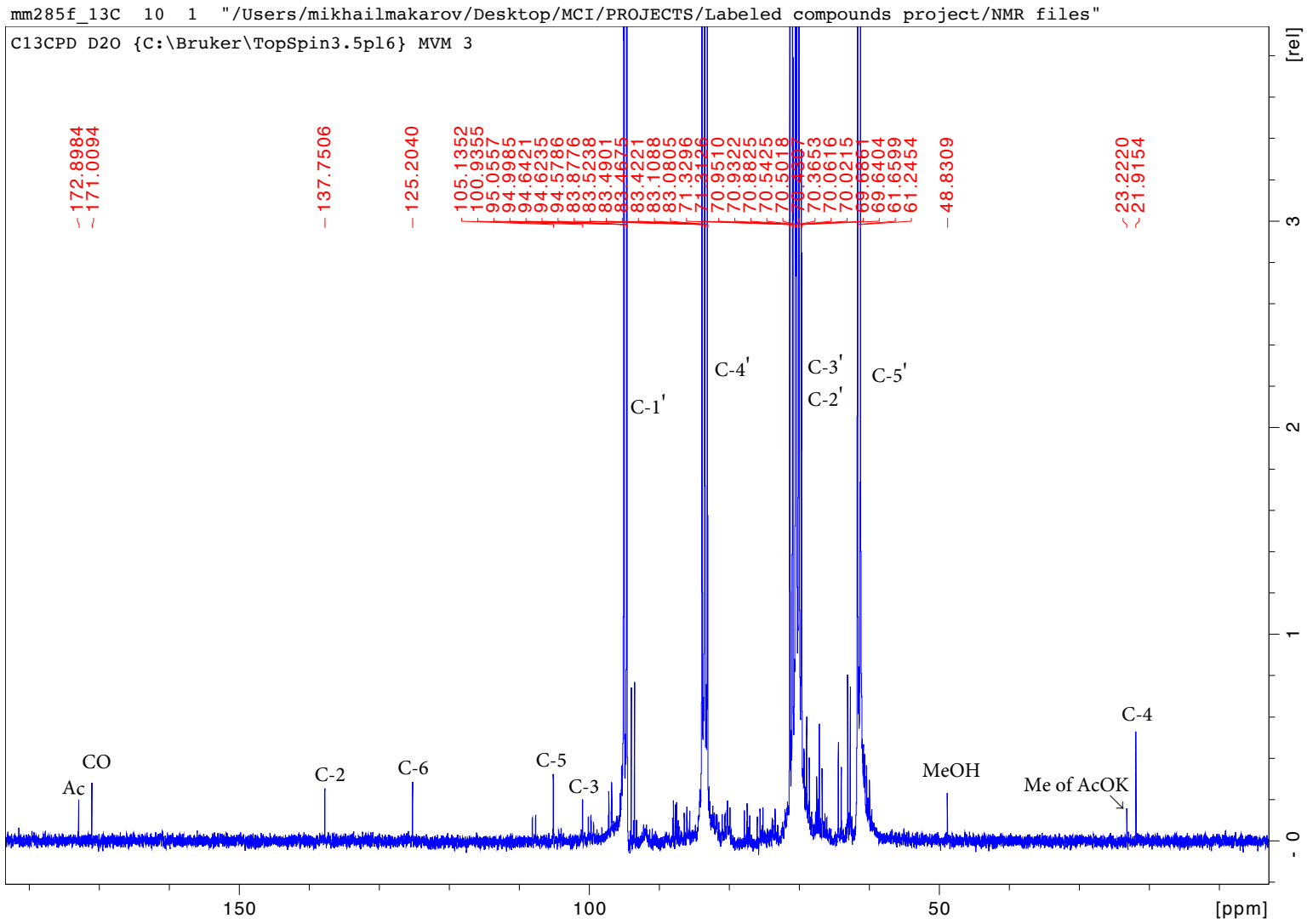



**Figure 85.** $^{13}C$ NMR ($D_2O$) of [$^{13}C_5$,$^{18}O$]NRH (m+7) (**13**).

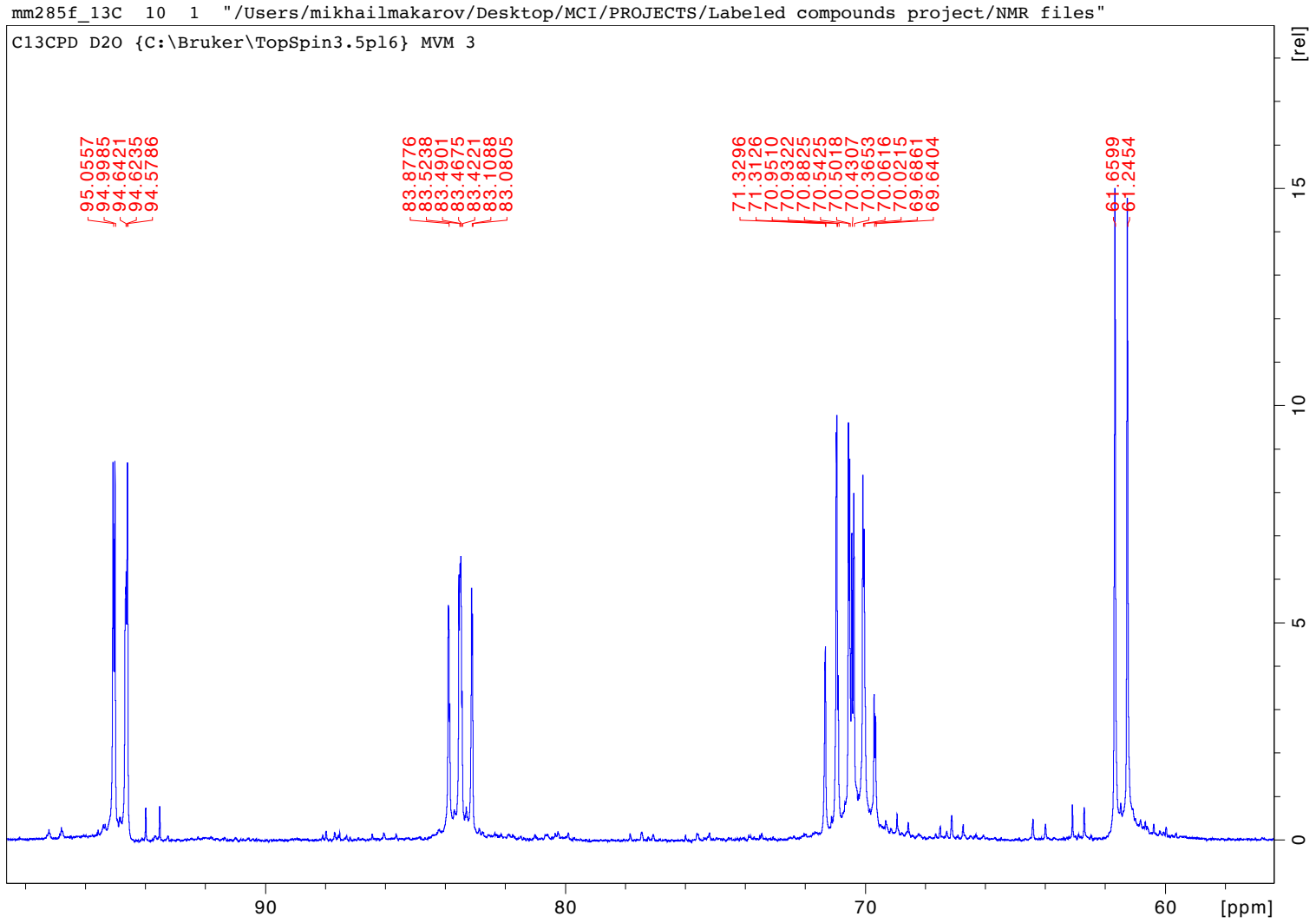



**Figure 86.** $^{13}C$ NMR ($D_2O$) of [$^{13}C_5$,$^{18}O$]NRH (m+7) (**13**), zoomed from 58 to 98 ppm (region of ribose redisue carbons).

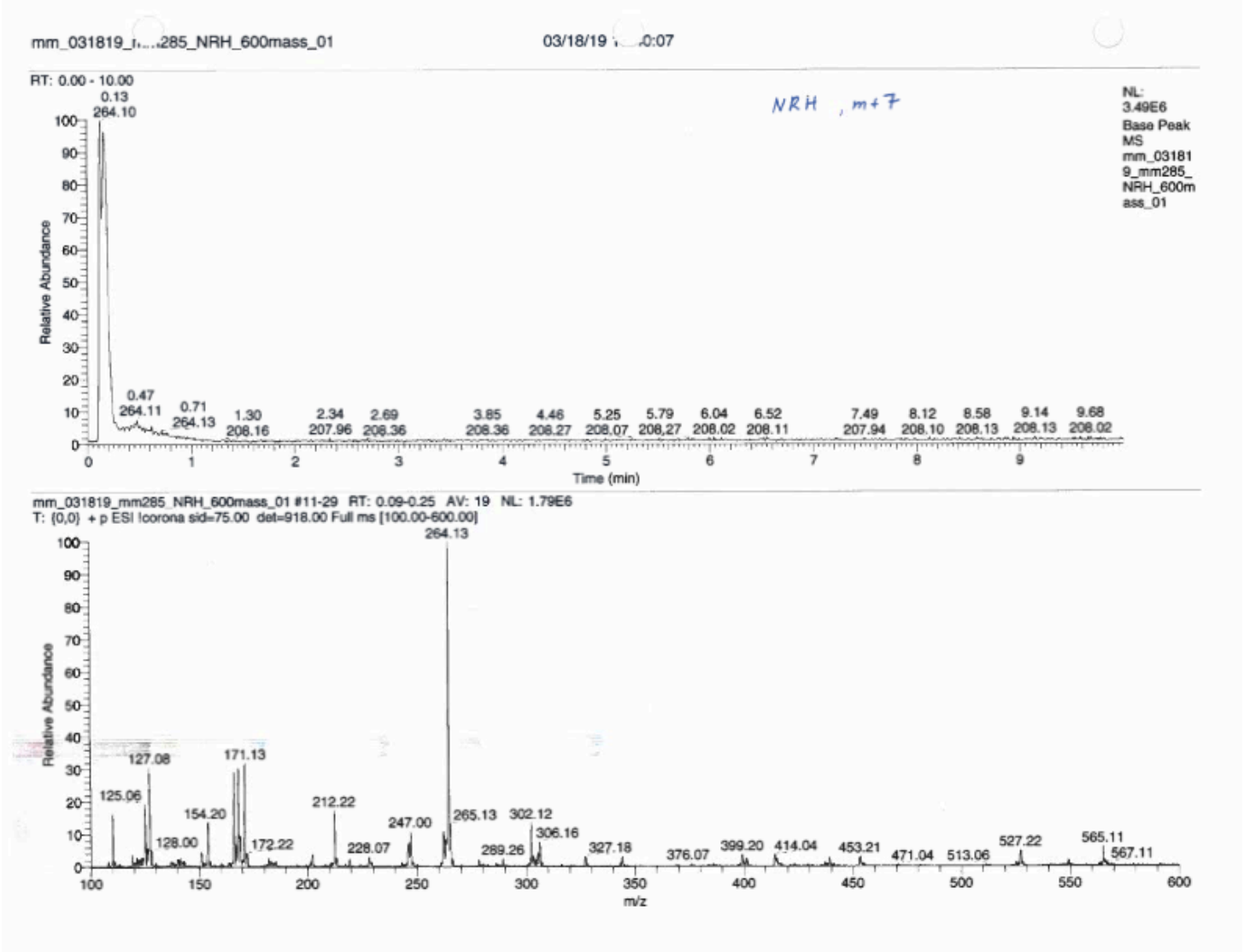



**Figure 87.** MS of [$^{13}C_5$,$^{18}O$]NRH (m+7) (**13**) in 1:1 $H_2O$/ACN.

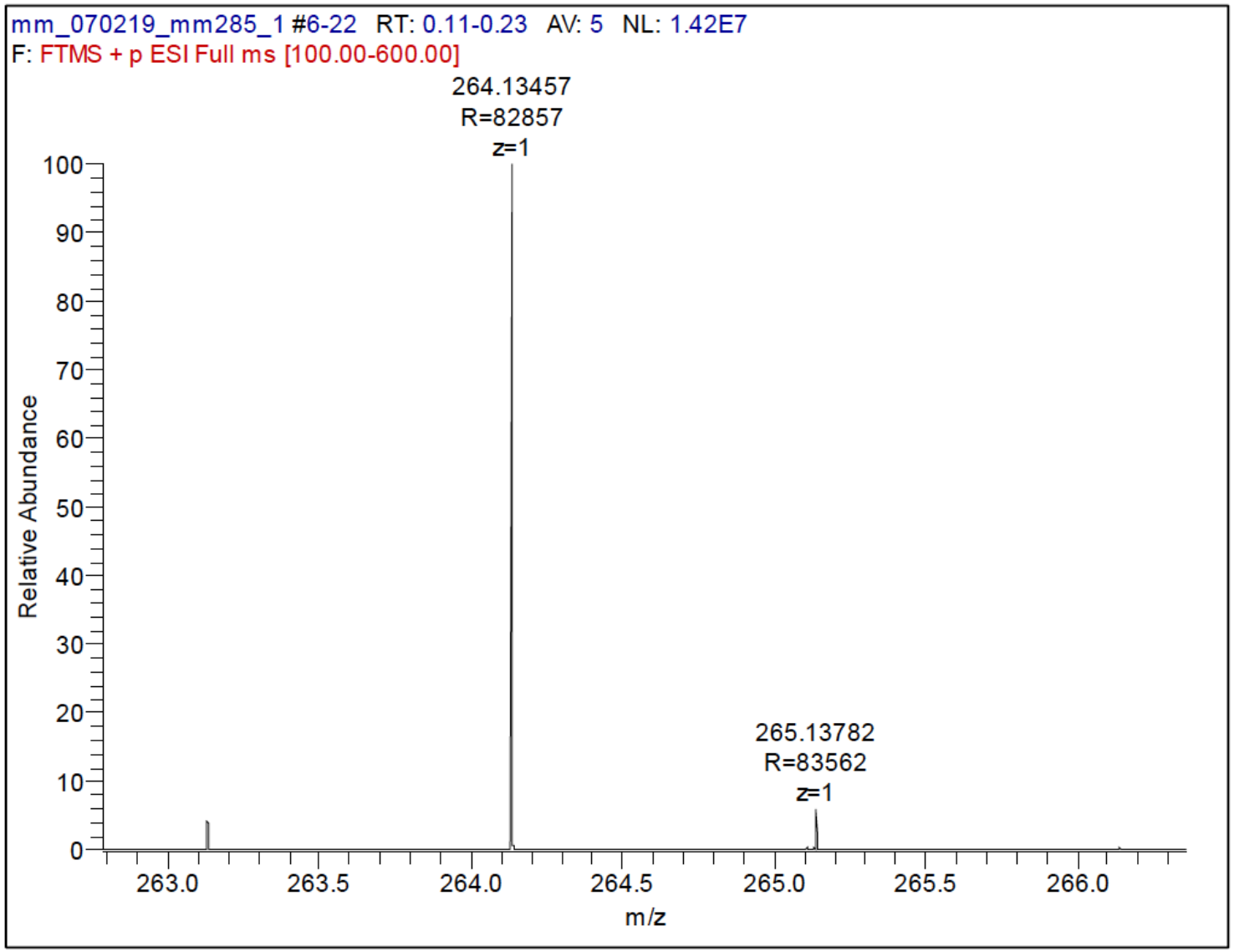



**Figure 88.** HRMS of [$^{13}C_5$,$^{18}O$]NRH (m+7) (**13**) in 1:1 $H_2O$/ACN.

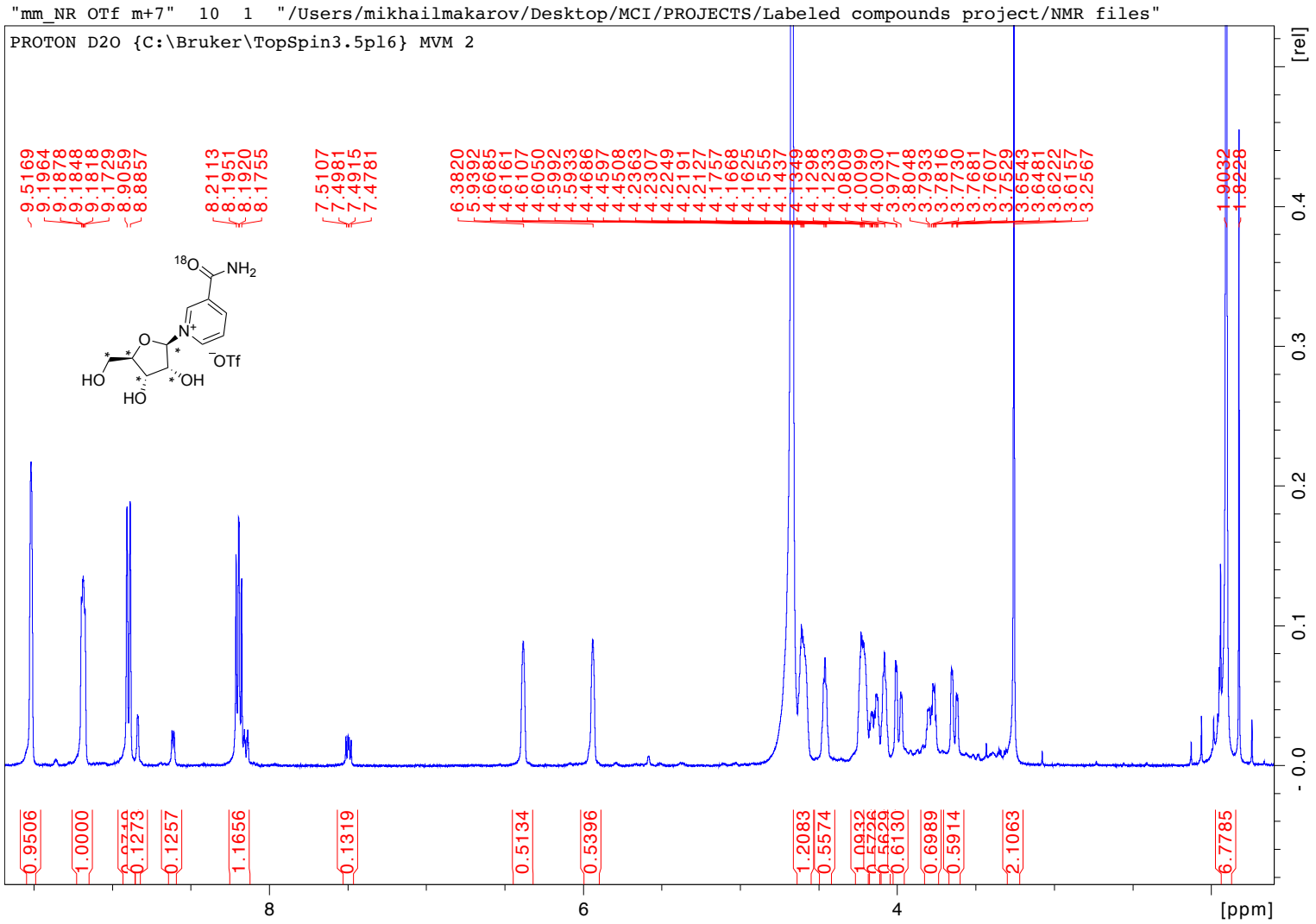



**Figure 89.** $^{1}H$ NMR ($D_2O$) of [$^{13}C_5$,$^{18}O$]NR OTf (m+7) (**11**), general view.

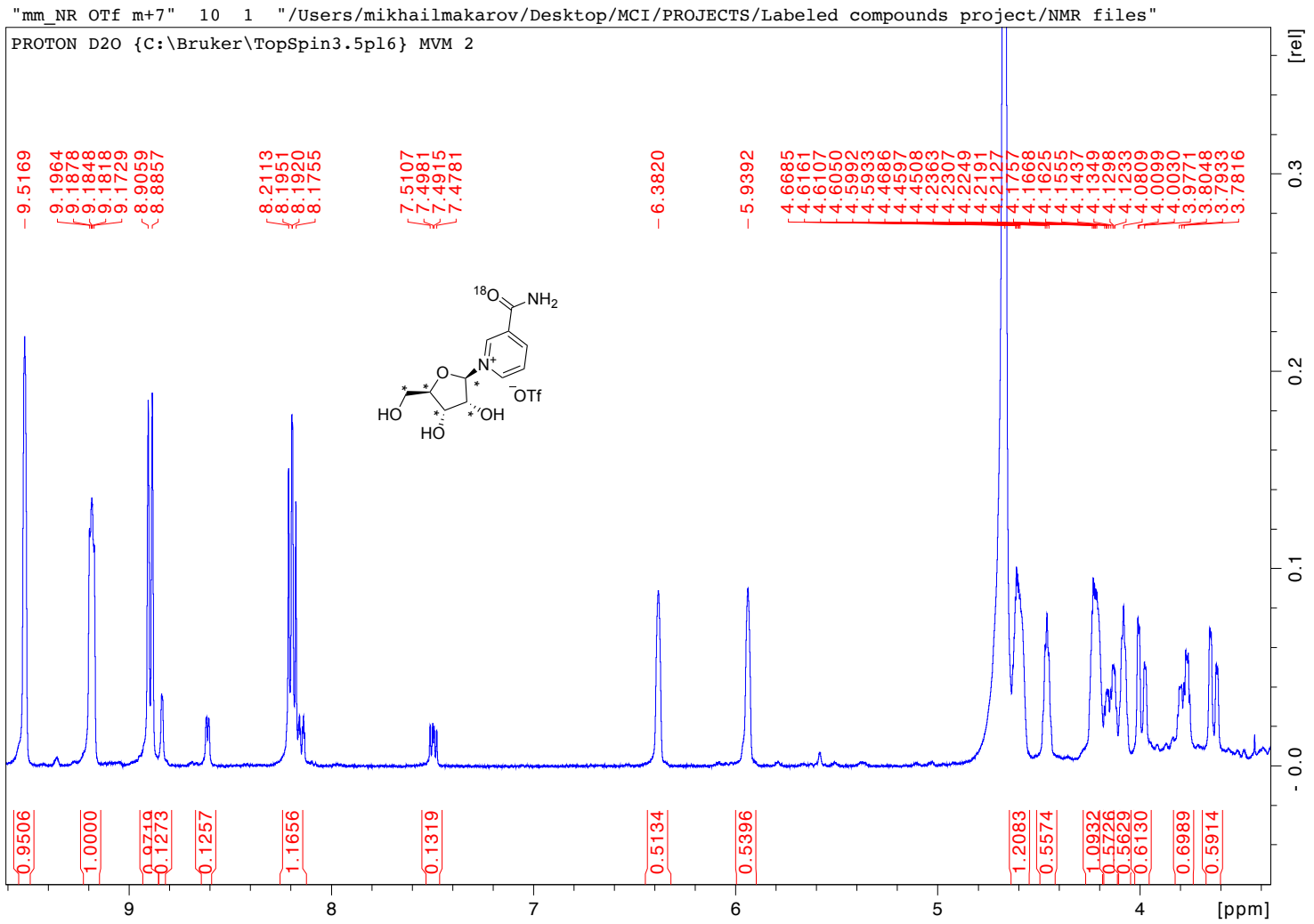



**Figure 90.** $^{1}H$ NMR ($D_2O$) of [$^{13}C_5$,$^{18}O$]NR OTf (m+7) (**11**), zoomed from 3.4 to 9.6 ppm.

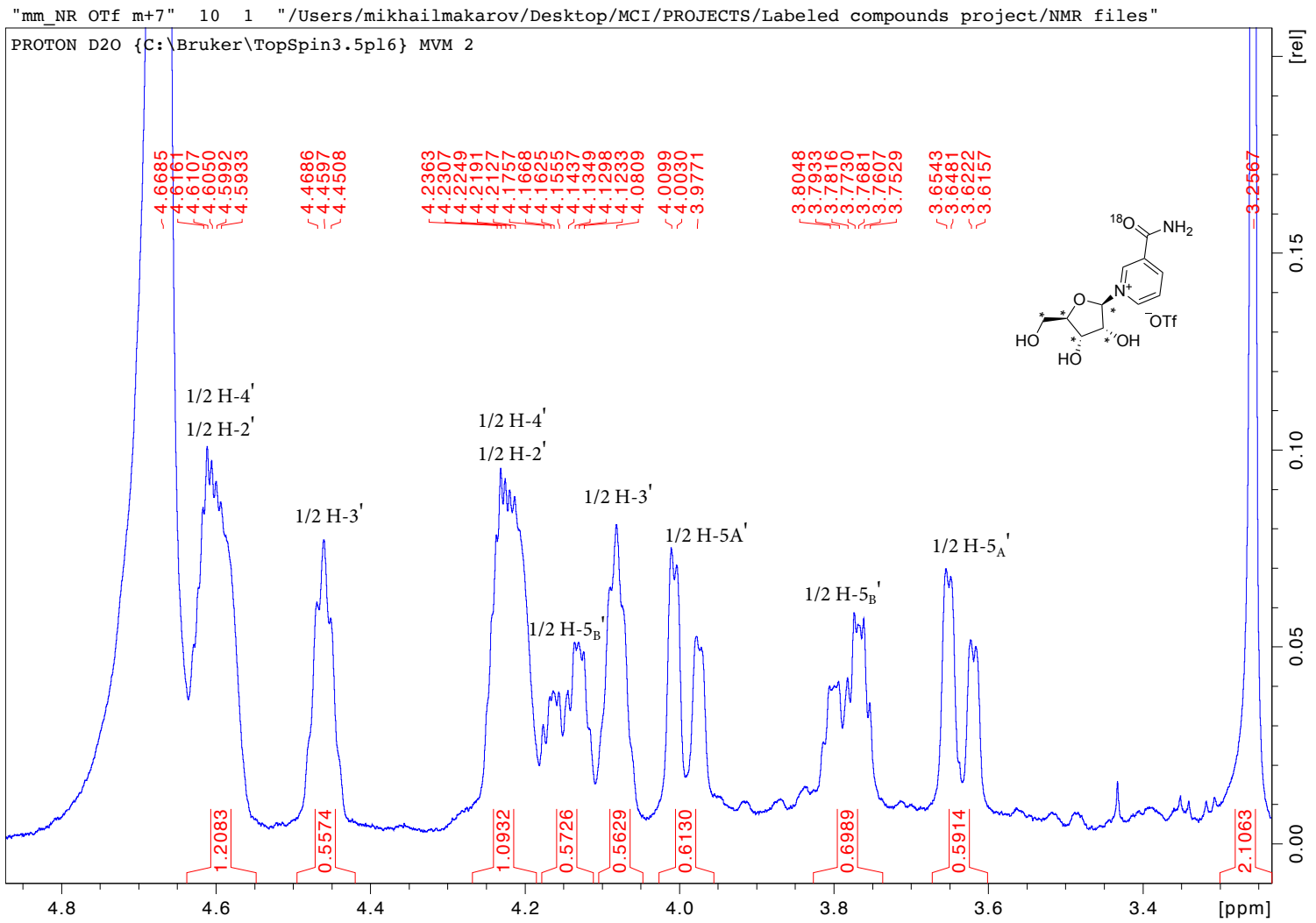



**Figure 91.** $^{1}H$ NMR ($D_2O$) of [$^{13}C_5$,$^{18}O$]NR OTf (m+7) (**11**), zoomed from 3.2 to 4.8 ppm.

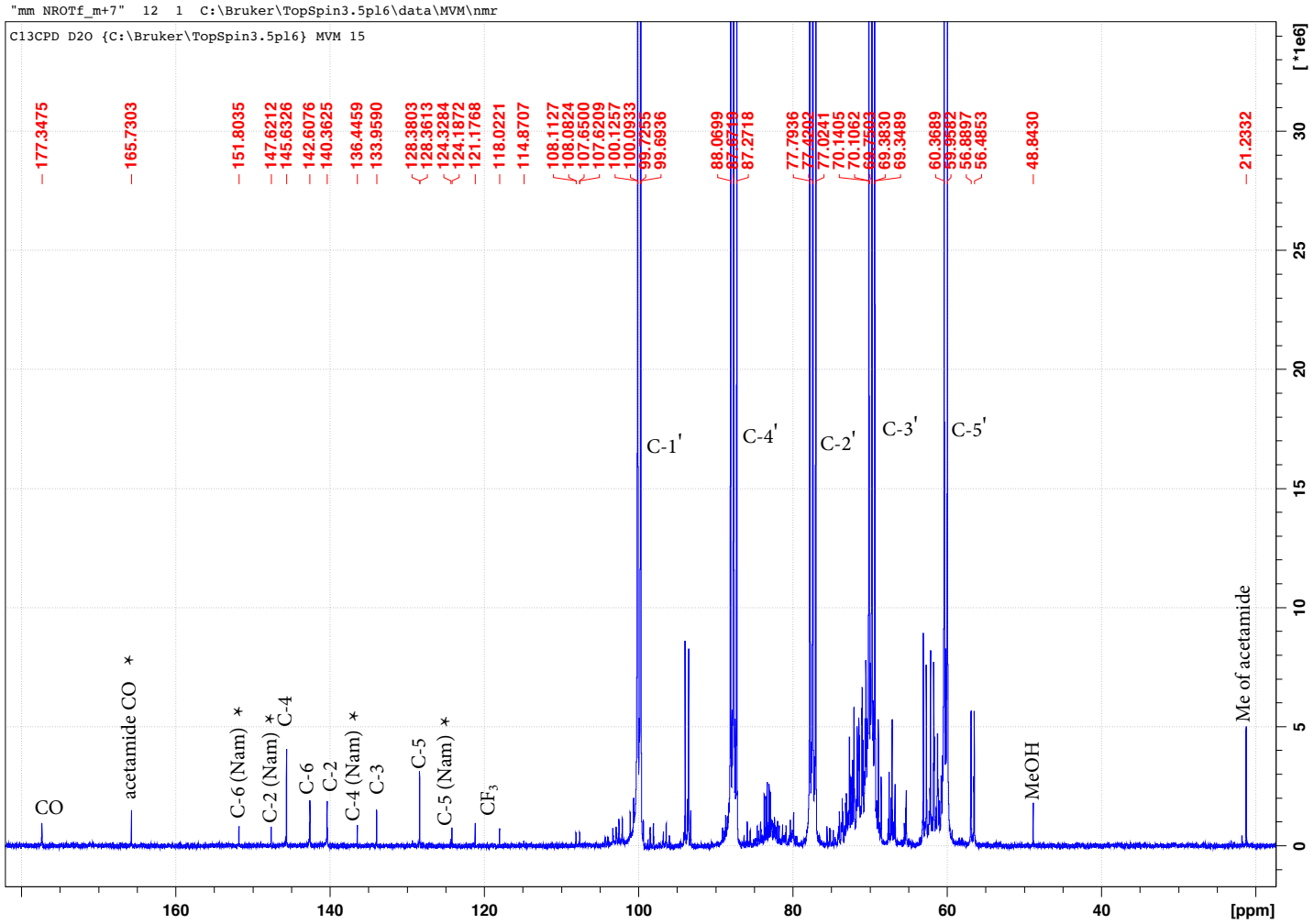



**Figure 92.** $^{13}C$ NMR ($D_2O$) of [$^{13}C_5$,$^{18}O$]NR OTf (m+7) (**11**), general view.

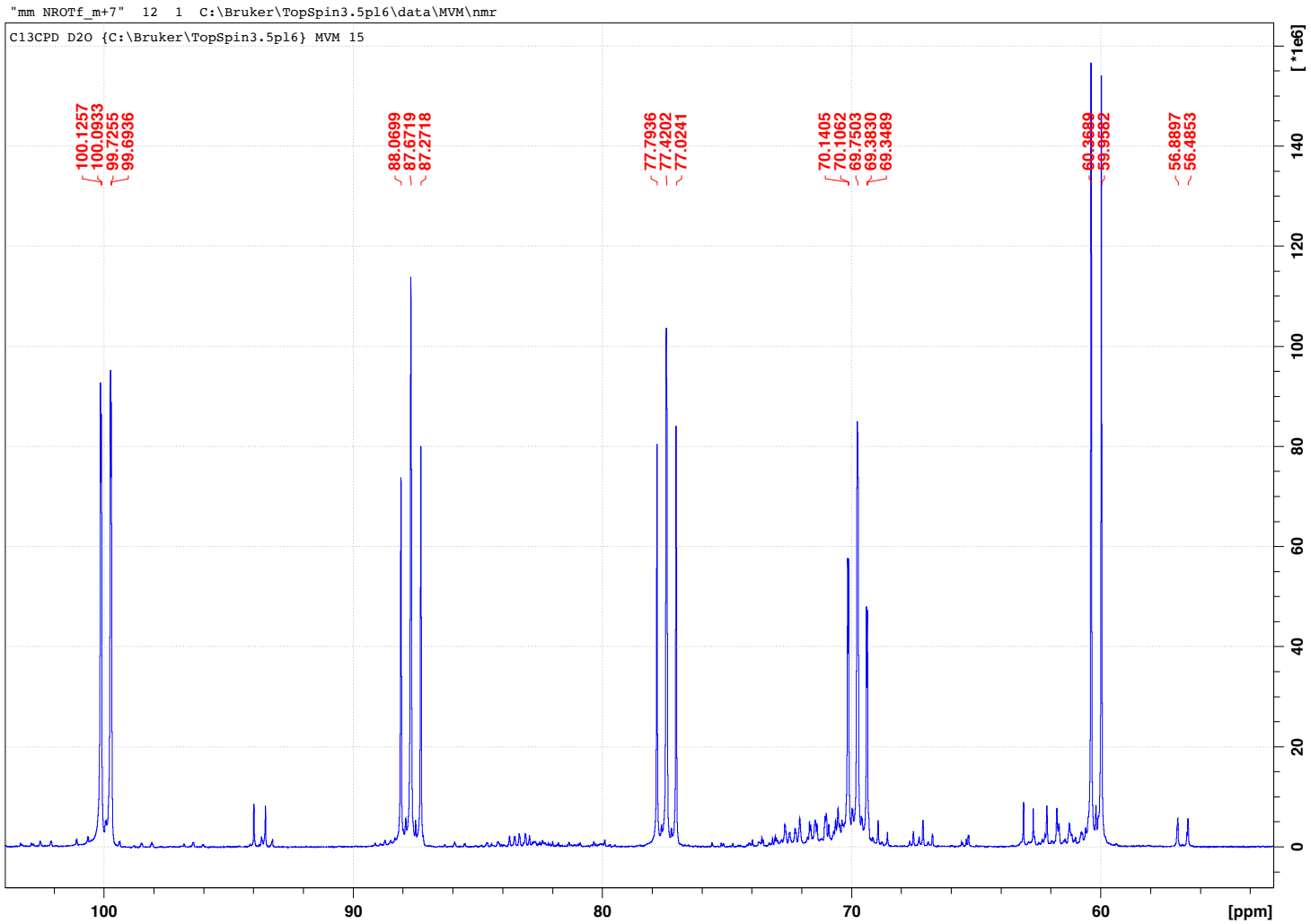



**Figure 93.** $^{13}C$ NMR ($D_2O$) of [$^{13}C_5$,$^{18}O$]NR OTf (m+7) (**11**), zoomed fron 54 to 102 ppm.

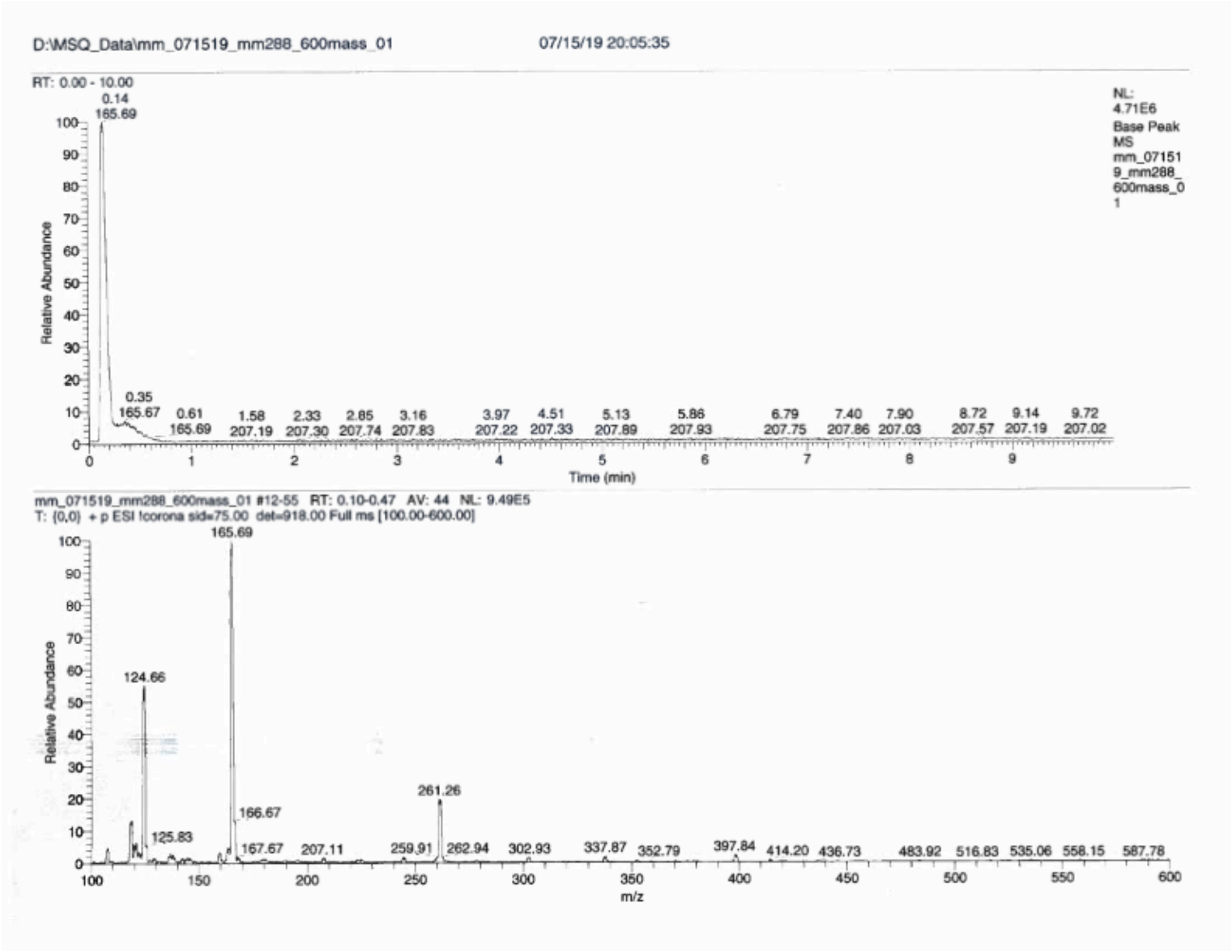



**Figure 94.** MS of [$^{13}C_5$,$^{18}O$]NR OTf (m+7) (**11**) in 1:1 $H_2O$/ACN.

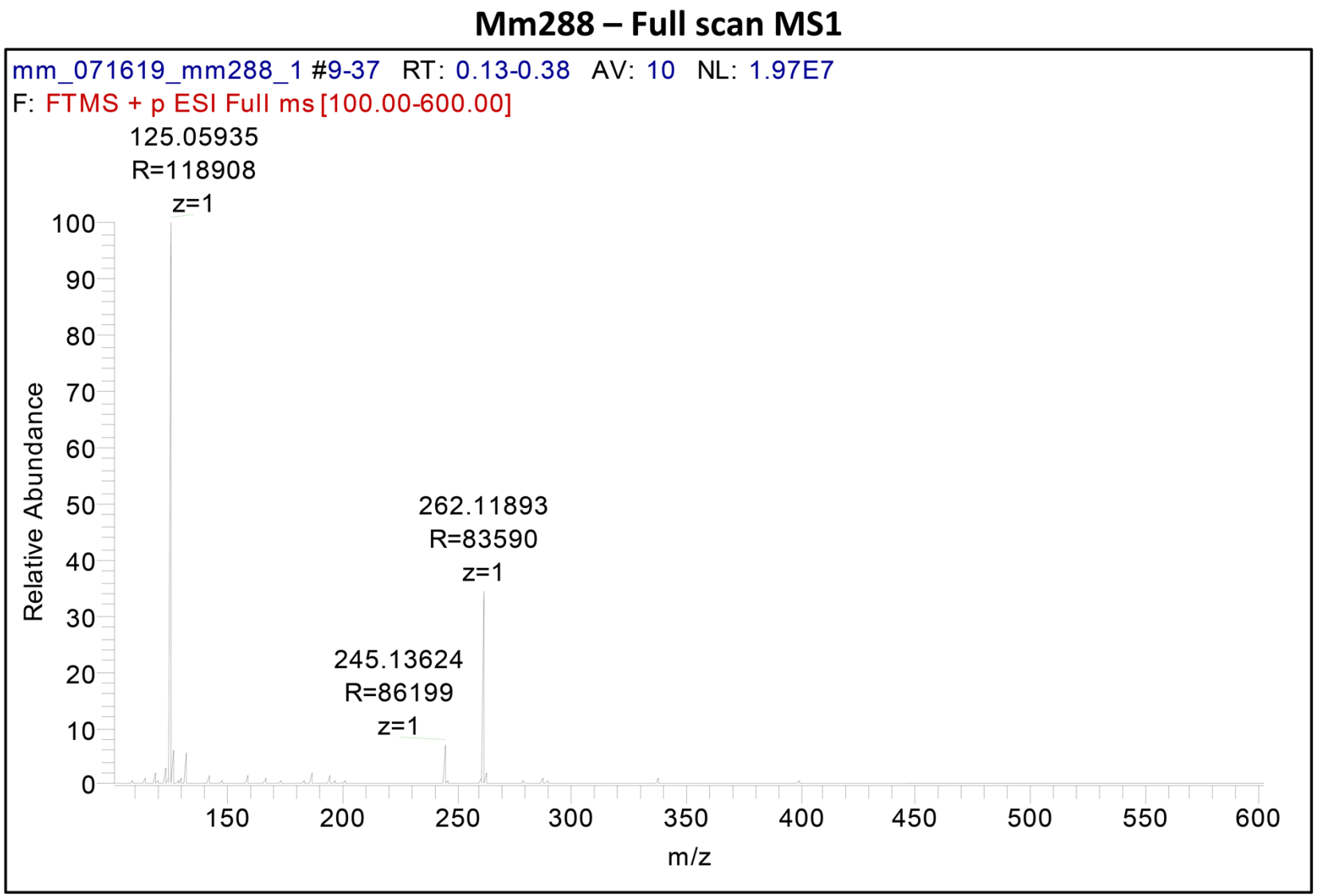



**Figure 95.** HRMS of [$^{13}C_5$,$^{18}O$]NR OTf (m+7) (**11**) in 1:1 $H_2O$/CAN, full scan.

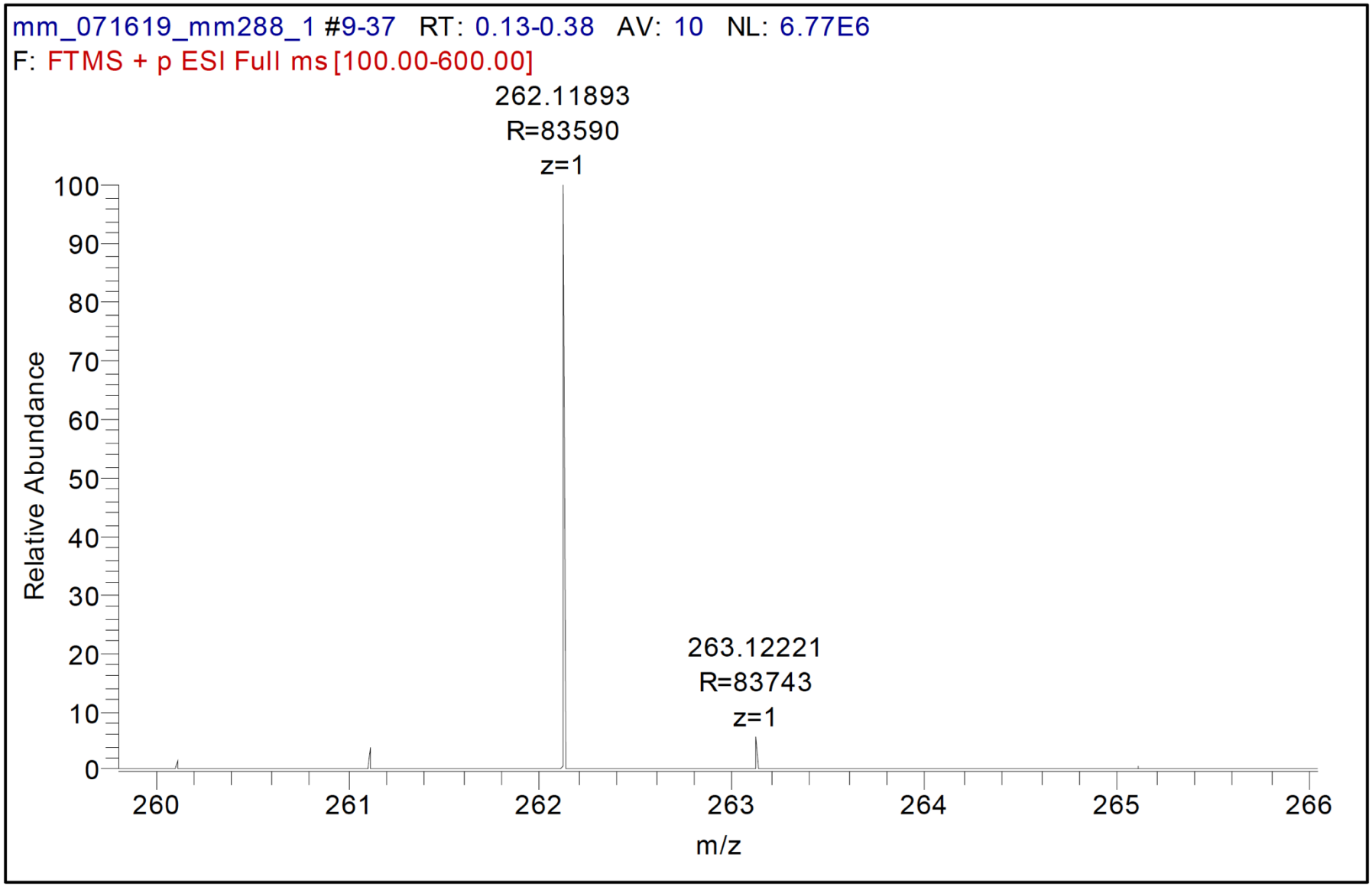



**Figure 96.** HRMS of [$^{13}C_5$,$^{18}O$]NR OTf (m+7) (**11**) in 1:1 $H_2O$/ACN.